REFERENCE TO A SEQUENCE LISTING SUBMITTED ON A COMPACT DISC

This application includes a Sequence Listing, which is provided as an electronic document on a compact disc (CD-R). This compact disc contains the file "Final Sequence Listing.txt" (6,125,872 bytes, created on January 19, 2010), which is hereby incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

Field of the Invention

[0002] This invention relates to the field of biology. In a particular embodiment, it relates to peptides, polynucleotides, and compositions useful to monitor or elicit an immune response to selected antigens, and methods of identifying such peptides and polynucleotides.

Related Art

- [0003] HLA class I molecules are expressed on the surface of almost all nucleated cells. Following intracellular processing of antigens, epitopes from the antigens are presented as a complex with the HLA class I molecules on the surface of such cells. CTL recognize the peptide-HLA class I complex, which then results in the destruction of the cell bearing the HLA-peptide complex directly by the CTL and/or via the activation of non-destructive mechanisms *e.g.*, the production of interferon, that inhibit viral replication.
- [0004] Human Immunodeficiency Virus. Acquired immunodeficiency syndrome (AIDS) caused by infection with human immunodeficiency virus-1 (HIV-1) represents a major world health problem. Estimates indicate that about 16,000 people worldwide are infected with HIV each day.
- [0005] The development of anti-viral drugs has been a major advancement in reducing viral loads in HIV infected patients. Highly active retroviral therapy (HAART) has been shown to reduce viremia to nearly undetectable levels. However, current drug therapies are not practicable as a long term solution to the HIV epidemic. HAART therapy is severely limited due to poor tolerance for the drugs and the emergence of drug-resistant virus. Moreover, replication competent HIV

persists in the lymphoid tissue of patients who have responded to HAART, thus serving as a reservoir of virus. Lastly, current anti-retroviral drug therapies have little impact upon the global epidemic: almost 90% of the world's HIV infected population resides within countries lacking financial resources for these drugs. Thus, a need exists for an efficacious vaccine to both prevent and treat HIV infection.

[0006] Virus-specific, human leukocyte antigen (HLA) class I-restricted cytotoxic T lymphocytes (CTL) are known to play a major role in the prevention and clearance of virus infections in vivo (Oldstone et al., Nature 321:239, 1989; Jamieson et al., J. Virol. 61:3930, 1987; Yap et al, Nature 273:238, 1978; Lukacher et al., J. Exp. Med. 160:814, 1994; McMichael et al., N. Engl. J. Med. 309:13, 1983; Sethi et al., J. Gen. Virol. 64:443, 1983; Watari et al., J. Exp. Med. 165:459, 1987; Yasukawa et al., J. Immunol. 143:2051, 1989; Tigges et al., J. Virol. 66:1622, 1993; Reddenhase et al., J. Virol. 55:263, 1985; Quinnan et al., N. Engl. J. Med. 307:6, 1982).

[0007] While immune correlates of protective immunity against HIV infection are not well defined, there is a growing body of evidence that suggests CTL are important in controlling HIV infection. HIV-specific CTL responses can be detected early in infection and the appearance of the responses corresponds to the time in infection at which initial viremia is reduced (Pantaleo et al., Nature 370:463, 1994; Walker et al., Proc. Natl. Acad. Sci. 86:9514, 1989). In addition, HIV replication in infected lymphocytes can be inhibited by incubation with autologous CTL (see, e.g., Tsubota et al., J. Exp. Med. 169:1421, 1989). These data are supported by recent studies that indicate CTL are required for controlling viral replication in a SIV/rhesus animal model (Schmitz et al., Science 283:857, 1999), and additionally supported by studies that demonstrate that CTL exert selective pressure on HIV populations as evidenced by the eventual predominance of viruses with amino acid replacements in those regions of the virus to which CTL responses are directed (see, e.g., Borrow et al., Nature Med. 3:205-211, 1997; Price et al., Proc. Nat. Acad. Sci. 94:12890-1895, 1997; Koenig et al., Nature Med. 1:330-336, 1995; and Haas et al., J. Immunol. 157:4212-4221, 1996).

[0008] Virus-specific T helper lymphocytes are also known to be critical for maintaining effective immunity in chronic viral infections. Historically, HTL responses were viewed as primarily supporting the expansion of specific CTL and B cell populations; however, more recent data indicate that HTL may directly contribute to the control of virus replication. For example, a decline in CD4⁺ T cells and a corresponding loss in HTL function characterize infection with HIV (Lane et al., New Engl. J. Med. 313:79, 1985). Furthermore, studies in HIV infected patients have also shown that there is an inverse relationship between virus-specific HTL responses and viral load, suggesting that HTL play a role in viremia (see, e.g., Rosenberg et al., Science 278:1447, 1997).

- [0009] A fundamental challenge in the development of an efficacious HIV vaccine is the heterogeneity observed in HIV. The virus, like some other infectious agents including retroviruses, rapidly mutates during replication resulting in the generation of virus that can escape anti-viral therapy and immune recognition (Borrow et al., Nature Med. 3:205, 1997). In addition, HIV can be classified into a variety of subtypes that exhibit significant sequence divergence (see, e.g., Lukashov et al., AIDS 12:S43, 1998). In view of the heterogeneous nature of HIV, and the heterogeneous immune response observed with HIV infection, induction of a multi-specific cellular immune response directed simultaneously against multiple HIV epitopes appears to be important for the development of an efficacious vaccine against HIV. There is a need to establish such vaccine embodiments which elicit immune responses of sufficient breadth and vigor to prevent and/or clear HIV infection.
- [0010] Hepatitis B Virus. Chronic infection by hepatitis B virus (HBV) affects at least 5% of the world's population and is a major cause of cirrhosis and hepatocellular carcinoma (Hoofnagle, J., N. Engl. J. Med. 323:337, 1990; Fields, B. and Knipe, D., In: Fields Virology 2:2137, 1990). The World Health Organization lists hepatitis B as a leading cause of death worldwide, close behind chronic pulmonary disease, and more prevalent than AIDS. Chronic HBV infection can range from an asymptomatic carrier state to continuous hepatocellular necrosis and inflammation, and can lead to hepatocellular carcinoma.
- [0011] The immune response to HBV is believed to play an important role in controlling hepatitis B infection. A variety of humoral and cellular responses to different regions of the HBV nucleocapsid core and surface antigens have been identified. T cell mediated immunity, particularly involving class I human leukocyte antigen-restricted cytotoxic T lymphocytes (CTL), is believed to be crucial in combatting established HBV infection.
- [0012] Several studies have emphasized the association between self-limiting acute hepatitis and multispecific CTL responses (Penna, A. et al., *J. Exp. Med.* 174:1565, 1991; Nayersina, R. et al., *J. Immunol.* 150:4659, 1993). Spontaneous and interferon-related clearance of chronic HBV infection is also associated with the resurgence of a vigorous CTL response (Guidotti, L. G. et al., *Proc. Natl. Acad. Sci. USA* 91:3764, 1994). In all such cases the CTL responses are polyclonal, and specific for multiple viral proteins including the HBV envelope, core and polymerase antigens. By contrast, in patients with chronic hepatitis, the CTL activity is usually absent or weak, and antigenically restricted.

- The crucial role of CTL in resolution of HBV infection has been further underscored by studies using HBV transgenic mice. Adoptive transfer of HBV-specific CTL into mice transgenic for the HBV genome resulted in suppression of virus replication. This effect was primarily mediated by a non-lytic, lymphokine-based mechanism (Guidotti, L. G. et al., *Proc. Natl. Acad. Sci. USA* 91:3764, 1994; Guidotti, L. G., Guilhot, S., and Chisari, F. V. *J. Virol.* 68:1265, 1994; Guidotti, L. G. et al., *J. Virol.* 69:6158, 1995; Gilles, P. N., Fey, G., and Chisari, F. V., *J. Virol.* 66:3955, 1992).
- As is the case for HLA class I restricted responses, HLA class II restricted T cell responses are usually detected in patients with acute hepatitis, and are absent or weak in patients with chronic infection (Chisari, F. V. and Ferrari, C., *Annu. Rev. Immunol.* 13:29, 1995). HLA Class II responses are tied to activation of helper T cells (HTLs) Helper T lymphocytes, which recognize Class II HLA molecules, may directly contribute to the clearance of HBV infection through the secretion of cytokines which suppress viral replication (Franco, A. et al., *J. Immunol.* 159:2001, 1997). However, their primary role in disease resolution is believed to be mediated by inducing activation and expansion of virus-specific CTL and B cells.
- [0015] In view of the heterogeneous immune response observed with HBV infection, induction of a multi-specific cellular immune response directed simultaneously against multiple epitopes appears to be important for the development of an efficacious vaccine against HBV. There is a need to establish vaccine embodiments that elicit immune responses that correspond to responses seen in patients that clear HBV infection. Epitope-based vaccines appear useful.
- [0016] Hepatitis C Virus. Hepatitis C virus (HCV) infection is a global human health problem with approximately 150,000 new reported cases each year in the U.S. alone. HCV is a single stranded RNA virus, and is the etiological agent identified in most cases of non-A, non-B post-transfusion and post-transplant hepatitis, and is a common cause of acute sporadic hepatitis (Choo et al., Science 244:359, 1989; Kuo et al., Science 244:362, 1989; and Alter et al., in: Current Perspective in Hepatology, p. 83, 1989). It is estimated that more than 50% of patients infected with HCV become chronically infected and, of those, 20% develop cirrhosis of the liver within 20 years (Davis et al., New Engl. J. Med. 321:1501, 1989; Alter et al., in: Current Perspective in Hepatology, p. 83, 1989; Alter et al., New Engl. J. Med. 327:1899, 1992; and Dienstag, J. L. Gastroenterology 85:430,

1983). Moreover, the only therapy available for treatment of HCV infection is interferon- α . Most patients are unresponsive, however, and among the responders, there is a high recurrence rate within 6-12 months of cessation of treatment (Liang *et al.*, *J. Med. Virol.* 40:69, 1993). Ribaviron, a guanosine analog with a broad spectrum activity against many RNA and DNA viruses, has been shown in clinical trials to be effective against chronic HCV infection when used in combination with interferon- α (*see*, *e.g.*, Poynard *et al.*, *Lancet* 352:1426-1432, 1998; Reichard *et al.*, *Lancet* 351:83-87, 1998) However, the response rate is still well below 50%.

- lymphocytes (CTL) are known to play a major role in the prevention and clearance of virus infections in vivo (Oldstone et al., Nature 321:239, 1989; Jamieson et al., J. Virol. 61:3930, 1987; Yap et al, Nature 273:238, 1978; Lukacher et al., J. Exp. Med. 160:814, 1994; McMichael et al., N. Engl. J. Med. 309:13, 1983; Sethi et al., J. Gen. Virol. 64:443, 1983; Watari et al., J. Exp. Med. 165:459, 1987; Yasukawa et al., J. Immunol. 143:2051, 1989; Tigges et al., J. Virol. 66:1622, 1993; Reddenhase et al., J. Virol. 55:263, 1985; Quinnan et al., N. Engl. J. Med. 307:6, 1982).
- [0018] In view of the heterogeneous immune response observed with HCV infection, induction of a multi-specific cellular immune response directed simultaneously against multiple HCV epitopes appears to be important for the development of an efficacious vaccine against HCV. There is a need, however, to establish vaccine embodiments that elicit immune responses that correspond to responses seen in patients that clear HCV infection.
- [0019] Human Papillomavirus. Human papillomavirus (HPV) is a member of the papillomaviridae, a group of small DNA viruses that infect a variety of higher vertebrates. More than 80 types of HPVs have been identified. Of these, more than 30 can infect the genital tract. Some types, generally types 6 and 11, may cause genital warts, which are typically benign and rarely develop into cancer. Other strains of HPV, "cancer-associated", or "high-risk" types, can more frequently lead to the development of cancer. The primary mode of transmission of these strains of HPV is through sexual contact.
- [0020] The main manifestations of the genital warts are cauliflower-like condylomata acuminata that usually involve moist surfaces; keratotic and smooth papular warts, usually on dry surfaces; and subclinical "flat" warts, which are found on any mucosal or cutaneous

surface (Handsfield, H., Am. J. Med. 102(5A):16-20, 1997). These warts are typically benign but are a source of inter-individual spread of the virus (Ponten, J. & Guo, Z., Cancer Surv. 32:201-29, 1998). At least three HPV strains associated with genital warts have been identified: type 6a (see, e.g., Hofmann, K.J., et al., Virology 209(2):506-518, 1995), type 6b (see, e.g., Hofmann et al., supra) and type 11 (see, e.g., Dartmann, K. et al., Virology 151(1):124-130, 1986).

- [0021] Cancer-associated HPVs have been linked with cancer in both men and women; they include, but are not limited to, HPV-16, HPV-18, HPV-31, HPV-45, HPV-33 and HPV-56. Other HPV strains, including types 6 and 11 as well as others, e.g., HPV-5 and HPV-8, are less frequently associated with cancer. The high risk types are typically associated with the development of cervical carcinoma and premalignant lesions of the cervix in women, but are also associated with similar malignant and premalignant lesions at other anatomic sites within the lower genital or anogenital tract. These lesions include neoplasia of the vagina, vulva, perineum, the penis, and the anus. HPV infection has also been associated with respiratory tract papillomas, and rarely, cancer, as well as abnormal growth or neoplasia in other epithelial tissues. See, e.g. VIROLOGY, 2ND ED, Fields et al., Eds. Raven Press, New York, 1990, Chapters 58 and 59, for a review of HPV association with cancer.
- The HPV genome consists of three functional regions, the early region, the late region, and the "long control region". The early region gene products control viral replication, transcription and cellular transformation. They include the HPV E1 and E2 proteins, which play a role in HPV DNA replication, and the E6 and E7 oncoproteins, which are involved in the control of cellular proliferation. The late region include the genes that encode the structural proteins L1 and L2, which are the major and minor capsid proteins, respectively. The "long control region" contains such sequences as enhancer and promoter regulatory regions.
- [0023] HPV expresses different proteins at different stages of the infection, for example early, as well as late, proteins. Even in latent infections, however, early proteins are often expressed and are therefore useful targets for vaccine-based therapies. For example, high-grade dysplasia and cervical squamous cell carcinoma continue to express E6 and E7, which therefore can be targeted to treat disease at both early and late stages of infection.
- [0024] Treatment for HPV infection is often unsatisfactory because of persistence of virus after treatment and recurrence of clinically apparent disease is common. The treatment

may require frequent visits to clinics and is not directed at elimination of the virus but at clearing warts. Because of persistence of virus after treatment, recurrence of clinically apparent disease is common.

- [0025] Thus, a need exists for an efficacious vaccine to both prevent and treat HPV infection and to treat cancer that is associated with HPV infection. Effective HPV vaccines would be a significant advance in the control of sexually transmissable infections and could also protect against clinical disease, particularly cancers such as cervical cancer. (see, e.g., Rowen, P. & Lacey, C., Dermatologic Clinics 16(4):835-838, 1998).
- [0026] Virus-specific, human leukocyte antigen (HLA) class I-restricted cytotoxic T lymphocytes (CTL) are known to play a major role in the prevention and clearance of virus infections in vivo (Oldstone et al., Nature 321:239, 1989; Jamieson et al., J. Virol. 61:3930, 1987; Yap et al, Nature 273:238, 1978; Lukacher et al., J. Exp. Med. 160:814, 1994; McMichael et al., N. Engl. J. Med. 309:13, 1983; Sethi et al., J. Gen. Virol. 64:443, 1983; Watari et al., J. Exp. Med. 165:459, 1987; Yasukawa et al., J. Immunol. 143:2051, 1989; Tigges et al., J. Virol. 66:1622, 1993; Reddenhase et al., J. Virol. 55:263, 1985; Quinnan et al., N. Engl. J. Med. 307:6, 1982).
- [0027] Virus-specific T helper lymphocytes are also known to be critical for maintaining effective immunity in chronic viral infections. Historically, HTL responses were viewed as primarily supporting the expansion of specific CTL and B cell populations; however, more recent data indicate that HTL may directly contribute to the control of virus replication. For example, a decline in CD4⁺ T cells and a corresponding loss in HTL function characterize infection with HIV (Lane et al., New Engl. J. Med. 313:79, 1985). Furthermore, studies in HIV infected patients have also shown that there is an inverse relationship between virus-specific HTL responses and viral load, suggesting that HTL plays a role in viremia (see, e.g., Rosenberg et al., Science 278:1447, 1997).
- [0028] The development of vaccines with prophylactic and therapeutic efficacy against HPV is ongoing. Early vaccine development was hampered by the inability to culture HPV. With the introduction of cloning techniques and protein expression, however, some attempts have been made to stimulate humoral and CTL response to HPV (See, e.g., Rowen, P. & Lacey, C., Dermatologic Clinics 16(4):835-838 (1998)). Studies to date, however, have been inconclusive.
- [0029] Activation of T helper cells and cytotoxic lymphocytes (CTLs) in the development of vaccines has also been analyzed. Lehtinen, M., et al. for instance, has shown that some

peptides from the E2 protein of HPV type 16 activate T helper cells and CTLs (*Biochem. Biophys. Res. Commun.* 209(2):541-6 (1995). Similarly, Tarpey *et al*, has shown that some peptides from HPV type 11 E7 protein can stimulate human HPV-specific CTLs *in vitro* (*Immunology* 81:222-227 (1994)) and Borysiewicz *et al.* have reported a recombinant vaccinia virus expressing HPV 16 and HPV 17 E6 and E7 that stimulated CTL responses in at least one patient (*Lancet* 347:1347-1357, 1996).

- [0030] Plasmodium falciparum and Malaria. Malaria, which is caused by infection with the parasite Plasmodium falciparum (PF), represents a major world health problem. Approximately 500 million people in the world are at risk from the disease, with approximately 200 million people actually harboring the parasites. An estimated 1 to 2 million deaths occur each year due to malaria. (Miller et al., Science 234:1349, 1986).
- [0031] Fatal outcomes are not confined to first infections, and constant exposure is apparently a prerequisite for maintaining immunity. Naturally acquired sterile immunity is rare, if it exists at all. Accordingly, major efforts to develop an efficacious malaria vaccine have been undertaken.
- [0032] Human volunteers injected with irradiated PF sporozoites are resistant to subsequent sporozoite challenges, which demonstrates that development of a malaria vaccine is indeed immunologically feasible. Furthermore, these immune individuals developed a vigorous response, including antibodies, and cytotoxic T lymphocyte (CTL) and helper T lymphocyte (HTL) components, directed against multiple antigens. Reproducing the breadth and multiplicity of this response in a vaccine, however, is a task of large proportions. The epitope approach, as described herein, may represent a solution to this challenge, in that it allows the incorporation of various antibody, CTL and HTL epitopes, from various proteins, in a single vaccine composition.
- [0033] Anti-sporozoite antibodies are by themselves, in general, not completely efficacious in clearing the infection (Egan et al., Science 236:453, 1987). However, high concentrations of antibodies directed against the repeated region of the major B cell antigen of the sporozoite/circumsporozoite protein (CSP) have been shown to prevent liver cell infection in certain experimental models (Egan et al., Science 236:453, 1987; Potocnjak, P. et al., Science 207:71, 1980). The present inventors have shown that constructs encompassing CSP-repeat B cell epitopes and the optimized helper epitope PADRETM (San Diego, CA) are highly immunogenic, and can protect in vitro against

sporozoite invasion in both mouse and human liver cells, and protect mice in vivo against live sporozoite challenge (Franke et al., Vaccine 17:1201-1205, 1999)

- [0034] PF-specific CD4⁺ T cells also have a role in malarial immunity beyond providing help for B cell and CTL responses. Experiments by Renia *et al.* (Renia, *et al.*, *Proc. Natl. Acad. Sci. USA* 88:7963, 1991) demonstrated that HTLs directed against the *Plasmodium yoelli* CS protein could in fact adoptivley transfer protection against malaria.
- [0035] Considerable data implicate CTLs in protection against pre-erythrocytic-stage malaria. CD8⁺ CTLs can eliminate *Plasmodium berghei* or *Plasmodium yoelii*-infected mouse hepatocytes from in vitro culture in a major histocompatibility complex (MHC)-restricted and antigen-restricted manner (Hoffman *et al.*, *Science* 244:1078-1081, 1989; Weiss *et al.*, J. *Exp. Med.* 171:763-773, 1990). Further, it has also been shown that the immunity that developed in mice vaccinated with irradiated sporozoites is also dependent upon the present of CD8+ T cells. These T cells accumulate in inflammatory liver infiltrates subsequent to challenge. Passive transfer of circumsporozoite (CSP)-specific CTL clones as long as three hours after inoculation of sporozoites (*i.e.*, after the parasites have left the bloodstream and infected liver cells) were capable of protecting animals against infection (Romero *et al.*, *Nature* 341:323, 1989).
- [0036] It is notable that CTL-restricted responses directed against a single antigen are insufficient to protect mice with different MHC alleles, and a combination of multiple antigens was required even to protect mice from the most common laboratory strains of *Plasmodium*. These data indicate that a combination of epitopes form several antigens is necessary to elicit a protective CTL response.
- Indirect evidence that CTLs are important in protective immunity against Pf in humans has also accumulated. It has been reported that cytotoxic CD8⁺ T cells can be identified in humans immunized with PF sporozoites (Moreno, et al., Int. Immunol. 3:997, 1991). Further, humans immunized with irradiated sporozoites or naturally exposed to malaria can generate a CTL response to the pre-erythrocytic-stage antigens, CSP, sporozoite surface protein 2 (SSP2), liver-stage antigen-1 (LSA-1), and exported protein-1 (Exp-1) (see, e.g. Malik et al., Proc. Natl. Acad. Sci. USA 88, 3300-3304, 1991; Doolan et al., Int. Immunol. 3:511-516, 1991; Hill et al., Nature 360:434-439, 1992). Additionally, there is evidence that the polymorphism within the CSP may be the result of selection by CTLs of parasites that express variant forms (MCutchan and Water, Immunol. Lett. 25:23-26, 1990). This is based on the observation that the variation is nonsynonymous at the

nucleotide level, thereby indicating selective pressure at the protein level. The polymorphism primarily maps to identified CTL and T helper epitopes (Doolan *et al.*, *Int. Immunol.* 5:27-46, 1993); and CTL responses to some of the parasite variants do not cross-react (Hill *et al.*, *supra*). Finally, the MHC class I human leukocyte antigen (HLA)-Bw53 has been associated with resistance to severe malaria in The Gambia, and CTLs to a conserved epitope restricted by the HLA-Bw53 allele have been identified on *P. falciparum* LSA-1 (Hill *et al.*, *Nature* 352:595-600, 1991; Hill *et al.*, *Nature* 340:434-439, 1992). Since HLA-Bw53 is found in 15%-40% of the population of sub-Saharan Africa but in less than 1% of Caucasians and Asians, these data suggest evolutionary selection on the basis of protection against severe malaria.

- [0038] Thus, antibody, and both HLA class I and class II restricted responses directed against multiple sporozoite antigens appear to be involved in generating protective immunity to malaria. Furthermore, several important antigenic epitopes against which humoral and cellular immunity is focused have already been exactly delineated.
- [0039] In view of the heterogeneous immune response observed with PF infection, induction of a multi-specific cellular immune response directed simultaneously against multiple PF epitopes appears to be important for the development of an efficacious vaccine against PF. There is a need, however, to establish vaccine embodiments that elicit immune responses that correspond to responses seen in patients that clear PF infection.
- [0040] Epitope-Based Vaccines. The use of epitope-based vaccines has several advantages over current vaccines. The epitopes for inclusion in such a vaccine are to be selected from conserved regions of viral or tumor-associated antigens, in order to reduce the likelihood of escape mutants. The advantage of an epitope-based approach over the use of whole antigens is that there is evidence that the immune response to whole antigens is directed largely toward variable regions of the antigen, allowing for immune escape due to mutations. Furthermore, immunosuppressive epitopes that may be present in whole antigens can be avoided with the use of epitope-based vaccines.
- [0041] Additionally, with an epitope-based vaccine approach, there is an ability to combine selected epitopes (CTL and HTL) and additionally to modify the composition of the epitopes, achieving, for example, enhanced immunogenicity. Accordingly, the immune response can be modulated, as appropriate, for the target disease. Similar engineering of the response is not possible with traditional approaches.

- [0042] Another major benefit of epitope-based immune-stimulating vaccines is their safety. The possible pathological side effects caused by infectious agents or whole protein antigens, which might have their own intrinsic biological activity, is eliminated.
- [0043] An epitope-based vaccine also provides the ability to direct and focus an immune response to multiple selected antigens from the same pathogen. Thus, patient-by-patient variability in the immune response to a particular pathogen may be alleviated by inclusion of epitopes from multiple antigens from that pathogen in a vaccine composition. A "pathogen" may be an infectious agent or a tumor associated molecule.
- [0044] One of the most formidable obstacles to the development of broadly efficacious epitope-based immunotherapeutics has been the extreme polymorphism of HLA molecules. In the past, effective non-genetically biased coverage of a population has been a task of considerable complexity; such coverage has required that epitopes be used specific for HLA molecules corresponding to each individual HLA allele. Therefore, impractically large numbers of epitopes would been required in order to cover ethnically diverse populations. Recently, methods have been developed that allow the identification of epitopes that bind multiple HLA molecules. Therefore, epitope-based vaccines can be designed that contain epitopes which, either individually or in combination, bind a greater number of HLA molecules. The resulting epitope-based vaccines have a greater breadth of population coverage across one or more continents and even worldwide.
- [0045] Variation in Epitopes of Infectious Agents. A challenge in the development of effective vaccines against infectious agents such as hepatitis B virus (HBV) (47, 60) hepatitis C virus (HCV) (61-63), human papilloma virus (HPV) (64, 65) Plasmodium falciparum (66), and human immunodeficiency virus (HIV-1) is the protein sequence variation associated with different isolates. This variation is the result of gene sequence mutations. When such mutations occur in regions encoding epitopes recognized by cytotoxic T-lymphocytes (CTL), they provide a mechanism for escape of the agent from immune system control.
- [0046] HIV-1 represents an infectious agent with an especially high frequency of sequence variation. The sequence variation associated with HIV-1 proteins from related isolates, members of the same clades or types, as well as unrelated isolates, is well documented (1). Viral escape from CTL induced as the result of natural infection or vaccines was documented in nonhuman primate models where the mechanism behind this

escape was mutation of the primary anchor residues in dominant CTL epitopes (5-9). Viral escape from HIV-specific CTL has also been strongly implied by data obtained from HIV-1 infected individuals whose disease status change, including the transition from acute to chronic infection (10, 11), loss of stable control of viral replication and subsequent progression to AIDS (4, 12) or mother-to-child transmission (13). Thus, HIV-1 genetic and protein sequence variation represent a significant challenge to immune system-based control of viral replication, both within infected individuals and within populations.

- [0047] While the public health need for a vaccine against HIV-1 is well recognized and accepted, the genetic variation of HIV-1 isolates represents a highly significant obstacle (1, 14-16). Several strategies have been proposed, some of which include:
 - (1) Designing vaccines on HIV-1 types prevalent within small, well defined populations or geographical regions, such as individual countries or regions, and producing multiple different vaccines for exclusive use within these countries or regions (16).
 - (2) Use of HIV-1 ancestral or consensus sequences based on HIV types present in larger target populations, such as groups of neighboring countries or continents (15, 17-19).
 - (3) Incorporation of viral gene products obtained from multiple different virus isolates, representing diversely different types or clades, into a single 'multivalent' vaccine.
- Related vaccine design concepts that incorporate many of the advantages associated with the approaches described above are the use of highly conserved regions or epitopes derived from these regions as the basis of the vaccine. The logic behind this approach is that conserved regions of the viral genome are those that have been maintained through the evolution of HIV-1 because changes impact gene product function and general viral fitness. This theory is consistent with analyses of HIV-1 protein sequence data which demonstrated that CTL epitopes are concentrated in conserved regions and that regions devoid of CTL epitopes are the most variable (20). Additional support comes from published reports describing CTL responses, induced as the result of

natural infection or vaccination, that recognize viral proteins or epitopes common to viral isolates from diverse types or clades (21-26). Broad function CTL responses are also known to be correlated with slower progression to AIDS, at least for certain carefully studied populations (27, 28). Despite these reports and the clustering of CTL epitopes in conserved regions of HIV-1 gene products, amino acid sequence variation of analogous regions and epitopes from different viral isolates, both within the same type or clade and from different types, remains significant. There are currently no rules guiding the selection of conserved regions of CTL epitopes for use in vaccines other than the use of amino acid sequence identity (29).

[0049] A clear understanding of how CTL recognize pathogen infected cells has emerged over the past decade. It is now well established that small fragments of pathogen-derived proteins are generated, defined as peptide epitopes generally 8-11 amino acids in length, which bind to HLA-A, -B, or -C (human Class I Major Histocompatability Molecules) molecules expressed on the cell surface. Sequencing of naturally processed peptides bound to HLA molecules provided a means to identify the amino acid residues required for allele-specific epitope-peptide binding (30-32). Data obtained from X-ray crystallographic analysis of HLA-epitope peptide complexes, allowed for the identification and structural characterization of 'binding pockets' within the peptide binding cleft of HLA molecules. More refined epitope anchor motif definitions were then developed using data obtained from in vitro peptide-MHC binding assays. It is now well known that the main anchor residues typically occur at position 2 and the carboxyl terminus of peptides 8-11 amino acids in length, thus positions 8, 9, 10 or 11 (33-40). The definition of epitope peptide binding anchor motifs is the key to most, if not all, epitope prediction methods.

[0050] Initial CTL epitope identification methods were developed using common HLA alleles, such as HLA-A2.1. Motifs defined using different HLA molecules were found to be similar and this lead to the definition of HLA supertype families (41). The biological effect of this supertype relationship was first demonstrated for HIV-1 epitopes in a study where the HLA-A3 and -A11 epitope peptide binding patterns repertoires were demonstrated to be overlapping, not only with each other but also with HLA-A31, -A33 and -A*6801 (42). This binding specificity was defined as the HLA-A3 supertype. A significant overlap in peptide binding patterns was also demonstrated amongst several serologically distant HLA-B alleles (43, 44), and multiple HLA-A2 alleles (45, 46),

resulting in the definition of the HLA-B7 and HLA-A2 supertype families. Recognition of epitopes by CTL in a supertype manner has since been demonstrated to occur naturally in infectious diseases and cancer (47-53).

- While only two positions within CTL epitopes are typically characterized as the primary binding anchor positions, the amino acids that can serve as the anchor residues are more variable. The preferred and tolerated amino acids that can serve as anchor residues for the HLA-A2, -A3 and -B7 supertype families of epitopes are listed in Table 1. It is possible for analogous HIV-1 epitope peptides derived from different isolates, which differ with respect to the amino acids used as anchor residues, to bind to HLA molecules similarly. This type of variation can be as conserved since it is likely that CTL produced against one epitope would recognize the related epitope. Thus, variation limited to changes in anchor residues that result in sufficient epitope peptide binding to HLA molecules does not result in immune escape from CTL. Epitopes that contain this type of variation can be identified using the appropriately designed motif search algorithms.
- The TCR of CTL has been reported to be somewhat flexible or promiscuous with respect to recognition of epitope peptides bound to HLA molecules. For HIV-1, this flexibility was demonstrated as CTL recognition of related, but slightly variable, epitopes by single clones of CTL produced following natural infection (54, 55). Similar flexibility of CTL epitope recognition was demonstrated using rhesus macaques and natural infection with SIV or immunization (56, 57). This observation is not unique to HIV-1 and SIV but rather the TCR appears to have evolved to allow promiscuous recognition of peptide epitope bound to MHC molecules (58).
- [0053] Selective replacement of certain amino acids in CTL epitope peptides, amino acids thought to represent TCR contact points, is not only tolerated but can increase the recognition of the epitopes by CTL clones (59). The types of amino acid substitutions that can be incorporated, typically amino acids that are similar in chemical properties are best tolerated, and their positions, independent of primary anchor positions, within a selected number of CTL epitopes from tumor associated antigens were also defined.
- [0054] For HIV-1 and other infectious agents, reproducible methods for predicting the CTL recognition of related variant epitopes that occur amongst isolates have not been developed. Nor have methods for identifying CTL epitopes that are most likely to induce broadly functional responses when used in vaccine. Thus, there exists a need to develop

such methods to overcome the challenge associated with protein sequence variation in HIV and other infectious agents.

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SUMMARY OF THE INVENTION

- [0055] The present invention is directed to methods for selecting a variant of a peptide epitope which induces a CTL response against another variant(s) of the peptide epitope, by determining whether the variant comprises only conserved residues, as defined herein, at non-anchor positions in comparison to the other variant(s).
- [0056] In some embodiments, antigen sequences from a population of an infectious agent, said antigens comprising variants of a peptide epitope, are optionally aligned (manually or by computer) along their length, preferably their full length. Variant(s) of a peptide epitope (preferably naturally occurring variants), each 8-11 amino acids in length and comprising the same MHC class I supermotif or motif, are identified manually or with the aid of a computer. In some embodiments, a variant is optionally chosen which comprises preferred anchor residues of said motif and/or which occurs with high frequency within the population of variants. In other embodiments, a variant is randomly chosen. The randomly or otherwise chosen variant is compared to from one to all the remaining variant(s) to determine whether it comprises only conserved residues in the non-anchor positions relative to from one to all the remaining variant(s).
- [0057] The present invention is also directed to variants identified by the methods above; peptides comprising such variants; nucleic acids encoding such variants and peptides; cells comprising such variants, and/or peptides, and/or nucleic acids; compositions comprising such variants, and/or peptides, and/or nucleic acids, and/or cells; as well as therapeutic and diagnostic methods for using such variants, peptides, nucleic acids, cells, and compositions.

BRIEF DESCRIPTION OF THE DRAWINGS/FIGURES

- FIGS. 1A-1E. Recognition of variant peptides by CTL generated against a single epitope. Variant peptides were identified from 167 HIV strains for 5 HIV epitopes, 3 HLA-A2 restricted (Env 134, A, Gag 386, B, and Vpr 62, C) and 2 HLA-A11 restricted (Pol 98, D, and Env 47, E). These are listed according to their relationship to a previously determined parent (P) into single anchor substitutions (A), single non-anchor substitutions (NA) or multiple substitutions (M). Binding of each variant peptide is also shown. The number of viral sequences containing each variant peptide is shown in the column labeled # Isolates, and is reported for the total sequences, Clade B sequences (B), and Clade C sequences (C). Finally, the ability of CTL primed against the parent peptide to recognize the variant peptides is shown in the bar graphs.
- [0059] FIGS. 2A-2C. Characterization of the peptide-specific T cell lines. A. FACS analysis of the TCRs expressed by peptide -stimulated cells after 0, 1, and 5 peptide stimulations, using a panel of commercially available mAb for mouse TCR 2-14. B-C. Peptide affinity. Parent and variant peptides were titrated against CTL that had been stimulated 5 times with the parent peptide.
- [0060] FIGS. 2A-2B. Recognition of a panel of variant peptides by PBL from an HIV-infected individual.
- [0061] FIG 4. Prediction of immunological conservation. Gag 271 variants and their binding are shown, along with the number of isolates that express each variant. Immunological recognition was predicted for each variant based on two different choices in the immunizing peptide. On the right, the immunogenicity for each variant is shown.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

- [0062] The invention can be better understood with reference to the following definitions:
- [0063] An "antigen" refers to a polypeptide encoded by the genome of an infectious agent, or other another source, but preferably an infectious agent in the present invention.

Examples of HIV antigens include Env, Gag, Nef, Pol, Tat, Rev, Vif, Vpr, Vpu, p17, p24, p2, p7, p1, p6, Protease, RT, Integrase, and gp160 (preferably Env, Gag, Nef, Pol, Tat, Rev, Vif, Vpr, Vpu). Examples of HBV antigens include Core, Env, and Pol. Examples of HCV antigens include Core, E1, E2, Ns1, Ns2, Ns3, Ns4, and Ns5. Examples of HPV antigens include E1, E2, E3, E4, E5, E6, E7, L1, and L2. Examples of *Plasmodium falciparum* antigens include CSP, SSP2, Exp1, and LSA1.

[0064]

Throughout this disclosure, "binding data" results are often expressed in terms of "IC₅₀'s." IC₅₀ is the concentration of peptide in a binding assay at which 50% inhibition of binding of a reference peptide is observed. Given the conditions in which the assays are run (*i.e.*, limiting HLA proteins and labeled peptide concentrations), these values approximate K_D values. Assays for determining binding are described in detail, *e.g.*, in PCT publications WO 94/20127 and WO 94/03205, and other publications such Sidney *et al.*, *Current Protocols in Immunology* 18.3.1 (1998); Sidney, *et al.*, *J. Immunol.* 154:247 (1995); and Sette, *et al.*, *Mol. Immunol.* 31:813 (1994). It should be noted that IC₅₀ values can change, often dramatically, if the assay conditions are varied, and depending on the particular reagents used (*e.g.*, HLA preparation, *etc.*). For example, excessive concentrations of HLA molecules will increase the apparent measured IC₅₀ of a given ligand.

[0065]

Alternatively, binding is expressed relative to a reference peptide. Although as a particular assay becomes more, or less, sensitive, the IC_{50} 's of the peptides tested may change somewhat, the binding relative to the reference peptide will not significantly change. For example, in an assay run under conditions such that the IC_{50} of the reference peptide increases 10-fold, the IC_{50} values of the test peptides will also shift approximately 10-fold. Therefore, to avoid ambiguities, the assessment of whether a peptide is a good (i.e. high), intermediate, weak, or negative binder is generally based on its IC_{50} , relative to the IC_{50} of a standard peptide. The Tables included in this application present binding data in a preferred biologically relevant form of IC_{50} nM.

[0066]

Binding may also be determined using other assay systems including those using: live cells (e.g., Ceppellini et al., Nature 339:392 (1989); Christnick et al., Nature 352:67 (1991); Busch et al., Int. Immunol. 2:443 (1990); Hill et al., J. Immunol. 147:189 (1991); del Guercio et al., J. Immunol. 154:685 (1995)), cell free systems using detergent lysates (e.g., Cerundolo et al., J. Immunol. 21:2069 (1991)), immobilized purified MHC (e.g., Hill et al., J. Immunol. 152, 2890 (1994); Marshall et al., J. Immunol. 152:4946 (1994)), ELISA systems (e.g., Reay et al., EMBO J. 11:2829 (1992)), surface plasmon resonance (e.g., Khilko et al., J. Biol. Chem. 268:15425 (1993)); high flux soluble phase assays (Hammer et al., J. Exp. Med. 180:2353 (1994)), and measurement of class I MHC stabilization or assembly (e.g., Ljunggren et al., Nature 346:476 (1990);

Schumacher et al., Cell 62:563 (1990); Townsend et al., Cell 62:285 (1990); Parker et al., J. Immunol. 149:1896 (1992)).

- [0067] As used herein, "high affinity" with respect to HLA class I molecules is defined as binding with an IC₅₀ or K_D value, of 50 nM or less, "intermediate affinity" is binding with an IC₅₀ or K_D value of between 50 and about 500 nM, weak affinity is binding with an IC₅₀ or K_D value of between about 500 and about 5000 nM. "High affinity" with repect to binding to HLA class II molecules is defined as binding with an IC₅₀ or K_D value of 100 nM or less; "intermediate affinity" is binding with an IC₅₀ or K_D value of between about 100 and about 1000 nM.
- [0068] A "computer" or "computer system" generally includes: a processor and related computer programs; at least one information storage/retrieval apparatus such as a hard drive, a disk drive or a tape drive; at least one input apparatus such as a keyboard, a mouse, a touch screen, or a microphone; and display structure, such as a screen or a printer. Additionally, the computer may include a communication channel in communication with a network. Such a computer may include more or less than what is listed above.
- [0069] "Cross-reactive binding" indicates that a peptide is bound by more than one HLA molecule; a synonym is degenerate binding.
- [0070] A "cryptic epitope" elicits a response by immunization with an isolated peptide, but the response is not cross-reactive *in vitro* when intact whole protein, which comprises the epitope, is used as an antigen.
- [0071] The term "derived" when used to discuss an epitope is a synonym for "prepared." A derived epitope can be isolated from a natural source, or it can be synthesized in accordance with standard protocols in the art. Synthetic epitopes can comprise artificial amino acids "amino acid mimetics," such as D isomers of natural occurring L amino acids or non-natural amino acids such as cyclohexylalanine. A derived/prepared epitope can be an analog of a native epitope.
- [0072] A "diluent" includes sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred diluent for pharmaceutical compositions. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as diluents, particularly for injectable solutions.
- [0073] A "dominant epitope" is an epitope that induces an immune response upon immunization with a whole native antigen (see, e.g., Sercarz, et al., Annu. Rev. Immunol. 11:729-766, 1993). Such a response is cross-reactive in vitro with an isolated peptide epitope.
- [0074] An "epitope" is the collective features of a molecule, such as primary, secondary and tertiary peptide structure, and charge, that together form a site recognized by an immunoglobulin, T cell receptor or HLA molecule. Alternatively, an epitope can be defined as a set of amino acid residues which is involved in recognition by a particular immunoglobulin, or in the context of T

cells, those residues necessary for recognition by T cell receptor proteins and/or Major Histocompatibility Complex (MHC) receptors. Epitopes are present in nature, and can be isolated, purified or otherwise prepared/derived by humans. For example, epitopes can be prepared by isolation from a natural source, or they can be synthesized in accordance with standard protocols in the art. Synthetic epitopes can comprise artificial amino acids, "amino acid mimetics," such as D isomers of naturally-occurring L amino acids or non-naturally-occurring amino acids such as cyclohexylalanine. Throughout this disclosure, epitopes may be referred to in some cases as peptides. The variants of the invention are set forth in Tables 6-9 and Figures 1A-4.

[0075]

It is to be appreciated that proteins or peptides that comprise a variant of the invention as well as additional amino acid(s) are still within the bounds of the invention. In certain embodiments, the peptide comprises a fragment of an antigen. A "fragment of an antigen" or "antigenic fragment" or simply "fragment" is a portion of an antigen which has 100% identity with a wild type antigen or naturally-ocurring variant thereof. The fragment may or may not comprise an epitope of the invention. The fragment may be less than or equal to 600 amino acids, less than or equal to 500 amino acids, less than or equal to 400 amino acids, less than or equal to 250 amino acids, less than or equal to 100 amino acids, less than or equal to 85 amino acids, less than or equal to 75 amino acids, less than or equal to 65 amino acids, or less than or equal to 50 amino acids in length. In certain embodiments, a fragment is e.g., less than 101 or less than 51 amino acids in length, in any increment down to 5 amino acids in length. For example, the fragment may be 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 amino acids in length.

[0076]

In certain embodiments, there is a limitation on the length of a peptide of the invention. The embodiment that is length-limited occurs when the protein/peptide comprising an epitope of the invention comprises a region (i.e., a contiguous series of amino acids) having 100% identity with a native sequence. In order to avoid the definition of epitope from reading, e.g., on whole natural molecules, there is a limitation on the length of any region that has 100% identity with a native peptide sequence. Thus, for a peptide comprising an epitope of the invention and a region with 100% identity with a native peptide sequence, the region with 100% identity to a native sequence generally has a length of: less than or equal to 600 amino acids, often less than or equal to 500 amino acids, often less than or equal to 400 amino acids, often less than or equal to 250 amino acids, often less than or equal to 75 amino acids, often less than or equal to 65 amino acids, and often less than or equal to 50 amino acids. In certain embodiments, an "epitope" of the invention

is comprised by a peptide having a region with less than 51 amino acids that has 100% identity to a native peptide sequence, in any increment down to 5 amino acids.

- [0077] Accordingly, peptide or protein sequences longer than 600 amino acids are within the scope of the invention, so long as they do not comprise any contiguous sequence of more than 600 amino acids that have 100% identity with a native peptide sequence. For any peptide that has five contiguous residues or less that correspond to a native sequence, there is no limitation on the maximal length of that peptide in order to fall within the scope of the invention. It is presently preferred that a peptide of the invention (e.g., a peptide comprising an epitope of the invention) be less than 600 residues long in any increment down to eight amino acid residues.
- [0078] A peptide epitope occurring with "high frequency" is one that occurs in at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% of the infectious agents in a population. A "high frequency" peptide epitope is one of the more common in a population, preferably the first most common, second most common, third most common, or fourth most common in a population of variant peptide epitopes.
- [0079] "Human Leukocyte Antigen" or "HLA" is a human class I or class II Major Histocompatibility Complex (MHC) protein (see, e.g., Stites, et al., IMMUNOLOGY, 8TH ED., Lange Publishing, Los Altos, CA (1994).
- [0080] An "HLA supertype or HLA family", as used herein, describes sets of HLA molecules grouped on the basis of shared peptide-binding specificities. HLA class I molecules that share somewhat similar binding affinity for peptides bearing certain amino acid motifs are grouped into such HLA supertypes. The terms HLA superfamily, HLA supertype family, HLA family, and HLA xx-like molecules (where "xx" denotes a particular HLA type), are synonyms. See Tables 1-4.
- [0081] As used herein, "high affinity" with respect to HLA class I molecules is defined as binding with an IC₅₀, or K_D value, of 50 nM or less; "intermediate affinity" is binding with an IC₅₀ or K_D value of between about 50 and about 500 nM; "weak affinity" is binding with an IC₅₀ or K_D value between about 500 and about 5000 nM. "High affinity" with respect to binding to HLA class II molecules is defined as binding with an IC₅₀ or K_D value of 100 nM or less; "intermediate affinity" is binding with an IC₅₀ or K_D value of between about 100 and about 1000 nM. See "binding data."
- [0082] An "IC₅₀" is the concentration of peptide in a binding assay at which 50% inhibition of binding of a reference peptide is observed. Given the conditions in which the assays are run (*i.e.*, limiting HLA proteins and labeled peptide concentrations), these values approximate K_D values. See "binding data."
- [0083] The terms "identical" or percent "identity," in the context of two or more peptide sequences or antigen fragments, refer to two or more sequences or subsequences that are the same

or have a specified percentage of amino acid residues that are the same, when compared and aligned for maximum correspondence over a comparison window, as measured using a sequence comparison algorithm or by manual alignment and visual inspection.

[0084]

An "immunogenic" peptide or an "immunogenic" epitope or "peptide epitope" is a peptide that comprises an allele-specific motif or supermotif such that the peptide will bind an HLA molecule and induce a CTL and/or HTL response. Thus, immunogenic peptides of the invention are capable of binding to an appropriate HLA molecule and thereafter inducing a cytotoxic T lymphocyte (CTL) response, or a helper T lymphocyte (HTL) response, to the peptide.

[0085]

An "infectious agent" refers to a disease-causing microorganism, including viruses, bacteria, fungi, and protozoa against which a cellular immune response, preferably a CTL response, plays a role in acquired immunity. Examples of infectious agents include viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), human papillomma virus (HPV), Influenza virus, Dengue virus, Epstein-Barr virus, bacteria such as Mycobacterium tuberculosis and Chlamydia, fungi such as Candida albicans, Cryptococcus neoformans, Coccidoides spp., Histoplasma spp., and Aspergillus fumigatis, protozoa such as Plasmodium spp., including P. falciparum, Trypanosoma spp., Schistosoma spp., Leishmania spp and the like. Preferred infectious agents include HIV, HBV, HCV, HPV, Epstein-Barr virus, Plasmodium falciparum, Influenza virus and Dengue virus.

[0086]

The phrases "isolated" or "biologically pure" refer to material which is substantially or essentially free from components which normally accompany the material as it is found in its native state. Thus, isolated peptides in accordance with the invention preferably do not contain materials normally associated with the peptides in their *in situ* environment. An "isolated" epitope refers to an epitope that does not include the whole sequence of the antigen or polypeptide from which the epitope was derived. Typically the "isolated" epitope does not have attached thereto additional amino acids that result in a sequence that has 100% identity with a native sequence. The native sequence can be a sequence such as a tumor-associated antigen from which the epitope is derived. Thus, the term "isolated" means that the material is removed from its original environment (*e.g.*, the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or peptide present in a living animal is not isolated, but the same polynucleotide or peptide, separated from some or all of the coexisting materials in the natural system, is isolated. Such a polynucleotide could be part of a vector, and/or such a polynucleotide or peptide could be part of a composition, and still be "isolated" in that such vector or composition is not part of its natural environment. Isolated RNA molecules include *in vivo* or *in vitro* RNA

transcripts of the DNA molecules of the present invention, and further include such molecules produced synthetically.

"Major Histocompatibility Complex" or "MHC" is a cluster of genes that plays a role in control of the cellular interactions responsible for physiologic immune responses. In humans, the MHC complex is also known as the human leukocyte antigen (HLA) complex. For a detailed description of the MHC and HLA complexes, see, Paul, FUNDAMENTAL IMMUNOLOGY, 3RD ED., Raven Press, New York (1993).

[0088] The term "motif" refers to a pattern of residues in an amino acid sequence of defined length, preferably a peptide of less than about 15 amino acids in length, or less than about 13 amino acids in length, usually from about 8 to about 13 amino acids (e.g., 8, 9, 10, 11, 12, or 13) for a class I HLA motif and from about 6 to about 25 amino acids (e.g., 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25) for a class II HLA motif, which is recognized by a particular HLA molecule. Motifs are typically different for each HLA protein encoded by a given human HLA allele. These motifs often differ in their pattern of the primary and secondary anchor residues. See Tables 1-3.

[0089] A "native" or a "wild type" sequence refers to a sequence found in nature.

[0090] A "negative binding residue" or "deleterious residue" is an amino acid which, if present at certain positions (typically not primary anchor positions) in a peptide epitope, results in decreased binding affinity of the peptide for the peptide's corresponding HLA molecule.

[0091] The term "peptide" is used interchangeably with "oligopeptide" in the present specification to designate a series of residues, typically L-amino acids, connected one to the other, typically by peptide bonds between the α -amino and carboxyl groups of adjacent amino acids.

[0092] A "PanDR binding" peptide or "PADRE®" peptide (Epimmune, San Diego, CA) is a member of a family of molecules that binds more than one HLA class II DR molecule. The pattern that defines the PADRE® family of molecules can be referred to as an HLA Class II supermotif. A PADRE® molecule binds to HLA-DR molecules and stimulates *in vitro* and *in vivo* human helper T lymphocyte (HTL) responses. For a further definition of the PADRE® family, see copending application US serial Nos. 09/709,774, filed November 11, 2000; and 09/707,738, filed November 6, 2000; PCT publication Nos WO 95/07707, and WO 97/26784; U.S. Patent Nos. 5,736,142 issued April 7, 1998; 5,679,640, issued October 21, 1997; and 6,413,935, issued July 2, 2002.

[0093] "Pharmaceutically acceptable" refers to a generally non-toxic, inert, and/or physiologically compatible composition or component of a composition.

[0094] A "pharmaceutical excipient" or "excipient" comprises a material such as an adjuvant, a carrier, pH-adjusting and buffering agents, tonicity adjusting agents, wetting agents, preservatives, and the like. A "pharmaceutical excipient" is an excipient which is pharmaceutically acceptable.

[0095] A "primary anchor residue" is an amino acid at a specific position along a peptide sequence which is understood to provide a contact point between the immunogenic peptide and the HLA molecule. One, two or three, primary anchor residues within a peptide of defined length generally defines a "motif" for an immunogenic peptide. These residues are understood to fit in close contact with peptide binding grooves of an HLA molecule, with their side chains buried in specific pockets of the binding grooves themselves. In one embodiment of an HLA class I motif, the primary anchor residues are located at position 2 (from the amino terminal position) and at the carboxyl terminal position of a peptide epitope in accordance with the invention. The primary anchor positions for each motif and supermotif of HLA Class I are set forth in Tables 1-2. For example, analog peptides can be created by altering the presence or absence of particular residues in these anchor positions. Such analogs are used to modulate the binding affinity of an epitope comprising a particular motif or supermotif. A "preferred primary anchor residue" is an anchor residue of a motif or supermotif that is associated with optimal binding. Preferred primary anchor residues are indicated in bold-face in Tables 1-2. A "tolerated primary anchor residue" is an anchor residue of a motif or supermotif that is associated with binding to a lesser extent than a preferred residue. Tolerated primary anchor residues are indicated in italicized text in Tables 1-2.

[0096] "Promiscuous recognition" by a TCR is where a distinct peptide is recognized by the various T cell clones in the context of various HLA molecules. Promiscuous binding by an HLA molecule is synonymous with cross-reactive binding.

[0097] A "protective immune response" or "therapeutic immune response" refers to a CTL and/or an HTL response to an antigen derived from an antigen of an infectious agent, which in some way prevents or at least partially arrests disease symptoms, side effects or progression. The immune response may also include an antibody response which has been facilitated by the stimulation of helper T cells.

[0098] By "ranking" the variants in a population of peptide epitopes is meant ordering each variant by its frequency of occurrance relative to the other variants.

[0099] The term "residue" refers to an amino acid or amino acid mimetic incorporated into a peptide or protein by an amide bond or amide bond mimetic.

[00100] A "secondary anchor residue" is an amino acid at a position other than a primary anchor position in a peptide which may influence peptide binding. A secondary anchor residue occurs at a significantly higher frequency amongst HLA-bound peptides than would be expected by random

distribution of amino acids at a given position. A secondary anchor residue can be identified as a residue which is present at a higher frequency among high or intermediate affinity binding peptides, or a residue otherwise associated with high or intermediate affinity binding. The secondary anchor residues are said to occur at "secondary anchor positions." For example, analog peptides can be created by altering the presence or absence of particular residues in these secondary anchor positions. Such analogs are used to finely modulate the binding affinity of an epitope comprising a particular motif or supermotif. The terminology "fixed peptide" is generally used to refer to an analog peptide that has changes in primary anchore position; not secondary.

- [00101] A "subdominant epitope" is an epitope which evokes little or no response upon immunization with a whole antigen or a fragment of the whole antigen comprising a subdominant epitope and a dominant epitope, which comprise the epitope, but for which a response can be obtained by immunization with an isolated peptide, and this response (unlike the case of cryptic epitopes) is detected when whole antigen or a fragment of the whole antigen comprising a subdominant epitope and a dominant epitope is used to recall the response in vitro or in vivo.
- [00102] A "supermotif" is a peptide binding specificity shared by HLA molecules encoded by two or more HLA alleles. Preferably, a supermotif-bearing peptide is recognized with high or intermediate affinity (as defined herein) by two or more HLA antigens.
- [00103] "Synthetic peptide" refers to a peptide that is abtained from a non-natural source, e.g., is man-made. Such peptides may be produced using such methods as chemical synthesis or recombinant DNA technology. "Synthetic peptides" include "fusion proteins."
- As used herein, a "vaccine" is a composition used for vaccination, e.g., for prophylaxis or therapy, that comprises one or more peptides of the invention. There are numerous embodiments of vaccines in accordance with the invention, such as by a cocktail of one or more peptides; one or more peptides of the invention comprised by a polyepitopic peptide; or nucleic acids that encode such peptides or polypeptides, e.g., a minigene that encodes a polyepitopic peptide. The "one or more peptides" can include any whole unit integer from 1-150, e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, or 150 or more peptides of the invention. The peptides or polypeptides can optionally be modified, such as by lipidation, addition of targeting or other sequences. HLA class I-binding peptides of the invention can be linked to HLA class II-binding peptides, e.g., a PADRE® universal HTL-bindind peptide, to facilitate activation of both cytotoxic T lymphocytes and helper T lymphocytes. Vaccines can comprise peptide pulsed antigen presenting cells, e.g., dendritic cells.
- [00105] A "variant of a peptide epitope" refers to a peptide that is identified from a different viral strain at the same position in an aligned sequence, and that varies by one or

more amino acids from the parent peptide epitope. Examples of peptide epitope variants include those shown in Tables 6-9 and Figures 1A-4. A "variant of an antigen" refers to an antigen that comprises at least one variant of a peptide epitope. Examples of antigen variants include those listed by sequence and/or accession number in Tables 10-22. A "variant of an infectious agent" refers to an infectious agent whose genome encodes at least one variant of an antigen. Variants of infectious agents are related viral, bacterial, funagl, or protozoan strains or isolates that vary in sequence but cause the same disease symptoms. Examples of infectious agent variants include HIV Clade A, B, and C subtypes, HBV subtypes adr, ayr, adw, and ayw, HCV types 1, 2, 3, 4, 5, and 6, HPV strains 1-92 (preferably strains 16, 18, 31, 33, 45, 52, 56, and 58) (see Table 10, listing accession numbers for the complete genome sequences of 167 HIV variants; Table 22, showing an alignment of the complete polyprotein sequences of 50 HCV variants) (see also, Human Retroviruses and AIDS 2000: A Compilation and Analysis of Nucleic Acid and Amino Acid Sequences, Kuiken CL, et al., Eds. Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM).

[00106] The nomenclature used to describe peptides/proteins follows the conventional practice wherein the amino group is presented to the left (the N-terminus) and the carboxyl group to the right (the C-terminus) of each amino acid residue. When amino acid residue positions are referred to in a peptide epitope they are numbered in an amino to carboxyl direction with position one being the position closest to the amino terminal end of the epitope, or the peptide or protein of which it may be a part. In the formulae representing selected specific embodiments of the present invention, the amino- and carboxyl-terminal groups, although not specifically shown, are in the form they would assume at physiologic pH values, unless otherwise specified. In the amino acid structure formulae, each residue is generally represented by standard three letter or single letter designations. The L-form of an amino acid residue is represented by a capital single letter or a capital first letter of a three-letter symbol, and the D-form for those amino acids having D-forms is represented by a lower case single letter or a lower case three letter symbol. However, when three letter symbols or full names are used without capitals, they may refer to L amino acids. Glycine has no asymmetric carbon atom and is simply referred to as "Gly" or "G". The amino acid sequences of peptides set forth herein are generally designated using the standard single letter symbol. (A, Alanine; C, Cysteine; D, Aspartic Acid; E, Glutamic Acid; F, Phenylalanine; G, Glycine; H, Histidine; I, Isoleucine; K, Lysine; L, Leucine; M, Methionine; N, Asparagine; P, Proline; Q, Glutamine; R, Arginine; S, Serine; T, Threonine; V, Valine; W, Tryptophan; and Y, Tyrosine.) In addition to these symbols, "B"in the single letter abbreviations used herein

designates α -amino butyric acid. In some embodiments, α -amino butyric acid may be replaced with cysteine.

Acronyms used herein are as follows:

APC: Antigen presenting cell

CD3: Pan T cell marker

CD4: Helper T lymphocyte marker CD8: Cytotoxic T lymphocyte marker

CEA: Carcinoembryonic antigen (see, e.g., SEQ ID NO: 363)

CTL: Cytotoxic T lymphocyte

DC: Dendritic cells. DC functioned as potent antigen presenting cells by stimulating

cytokine release from CTL lines that were specific for a model peptide derived from hepatitis B virus. *In vivo* experiments using DC pulsed *ex vivo* with an HBV peptide epitope have stimulated CTL immune responses *in vivo* following delivery

to naïve mice.

DLT: Dose-limiting toxicity, an adverse event related to therapy.

DMSO: Dimethylsulfoxide

ELISA: Enzyme-linked immunosorbant assay

E:T: Effector:Target ratio

G-CSF: Granulocyte colony-stimulating factor

GM-CSF: Granulocyte-macrophage (monocyte)-colony stimulating factor

HBV: Hepatitis B virus

HER2/neu: A tumor associated antigen; c-erbB-2 is a synonym (see, e.g., SEQ ID NO: 364)

HLA: Human leukocyte antigen

HLA-DR: Human leukocyte antigen class II

HPLC: High Performance Liquid Chromatography

HTC: Helper T Cell

HTL: Helper T Lymphocyte. A synonym for HTC.

ID: Identity

IFNγ: Interferon gammaIL-4: Interleukin-4IV: Intravenous

LU_{30%}: Cytotoxic activity for 10⁶ effector cells required to achieve 30% lysis of a target

cell population, at a 100:1 (E:T) ratio.

MAb: Monoclonal antibody

MAGE: Melanoma antigen (see, e.g., SEQ ID NO: 365 and 366 for MAGE2 and MAGE3)

MLR: Mixed lymphocyte reaction

MNC: Mononuclear cells PB: Peripheral blood

PBMC: Peripheral blood mononuclear cell

ProGPTM: ProgenipoietinTM product (Searle, St. Louis, MO), a chimeric flt3/G-

CSF receptor agonist.

SC: Subcutaneous

S.E.M.: Standard error of the mean

OD: Once a day dosing

TAA: Tumor Associated Antigen
TNF: Tumor necrosis factor
WBC: White blood cells

[00107] The following describes the peptides, nucleic acid molecules, compositions, and methods of the invention in more detail.

Methods of Identifying Candidate Peptide Epitopes

[00108] The present invention is directed to methods for selecting a variant of a peptide epitope which induces a CTL response against another variant(s) of the peptide epitope, by determining whether the variant comprises only conserved residues, as defined herein, at non-anchor positions in comparison to the other variant(s).

[00109] In some embodiments, antigen sequences from a population of an infectious agent, said antigens comprising variants of a peptide epitope, are optionally aligned (manually or by computer) along their length, preferably their full length. Variant(s) of a peptide epitope (preferably naturally occurring variants), each 8-11 amino acids in length and comprising the same MHC class I supermotif or motif, are identified manually or with the aid of a computer. In some embodiments, a variant is optionally chosen which comprises preferred anchor residues of said motif and/or which occurs with high frequency within the population of variants. In other embodiments, a variant is randomly chosen. The randomly or otherwise chosen variant is compared to from one to all the remaining variant(s) to determine whether it comprises only conserved residues in the non-anchor positions relative to from one to all the remaining variant(s).

[00110] The present invention is also directed to variants identified by the methods above; peptides comprising such variants; nucleic acids encoding such variants and peptides; cells comprising such variants, and/or peptides, and/or nucleic acids; compositions comprising such variants, and/or peptides, and/or nucleic acids, and/or cells; as well as therapeutic and diagnostic methods for using such variants, peptides, nucleic acids, cells, and compositions.

[00111] In some embodiments, the invention is directed to a method for identifying a candidate peptide epitope which induces a HLA class I CTL response against variants of said peptide epitope, comprising

 a) identifying, from a particular antigen of an infectious agent, variants of a peptide epitope 8-11 amino acids in length, each variant comprising primary anchor residues of the same HLA class I binding motif; and

- b) determining whether one of said variants comprises only conserved non-anchor residues in comparison to at least one remaining variant, thereby identifying a candidate peptide epitope.
- [00112] In some embodiments, (b) comprises identifying a variant which comprises only conserved non-anchor residues in comparison to at least 25%, at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% of the remaining variants.
- [00113] In some embodiments, the invention is directed to a method for identifying a candidate peptide epitope which induces a HLA class I CTL response against variants of said peptide epitope, comprising
 - a) identifying, from a particular antigen of an infectious agent, variants of a peptide epitope 8-11 amino acids in length, each variant comprising primary anchor residues of the same HLA class I binding motif;
 - b) determining whether each of said variants comprises conserved, semiconserved or non-conserved non-anchor residues in comparison to each of the remaining variants; and
 - c) identifying a variant which comprises only conserved non-anchor residues in comparison to at least one remaining variant.
- [00114] In some embodiments, (c) comprises identifying a variant which comprises only conservative non-anchor residues in comparison to at least 25%, at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% of the remaining variants.
- [00115] In some embodiments, the invention is directed to a method for identifying a candidate peptide epitope which induces a HLA class I CTL response against variants of said peptide epitope, comprising
 - a) identifying, from a particular antigen of an infectious agent, a
 population of variants of a peptide epitope 8-11 amino acids in length,
 each peptide epitope comprising primary anchor residues of the same
 HLA class I binding motif;
 - b) choosing a variant selected from the group consisting of:
 - a variant which comprises preferred primary anchor residues
 of said motif; and

- ii) a variant which occurs with high frequency within the population of variants; and
- c) determining whether the variant of (b) comprises only conserved nonanchor residues in comparison to at least one remaining variant, thereby identifying a candidate peptide epitope.
- [00116] In some embodiments, (c) comprises identifying a variant which comprises only conservative non-anchor residues in comparison to at least 25%, at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% of the remaining variants.
- [00117] In some embodiments, the invention is directed to method for identifying a candidate peptide epitope which induces a HLA class I CTL response against variants of said peptide epitope, comprising
 - a) identifying, from a particular antigen of an infectious agent, a
 population of variants of a peptide epitope 8-11 amino acids in length,
 each peptide epitope comprising primary anchor residues of the same
 HLA class I binding motif;
 - b) choosing a variant selected from the group consisting of:
 - a variant which comprises preferred primary anchor residues of said motif; and
 - ii) a variant which occurs with high frequency within the population of variants; and
 - c) determining whether the variant of (b) comprises conserved, semiconserved or non-conserved non-anchor residues in comparison to each of the remaining variants; and
 - d) identifying a variant which comprises only conserved non-anchor residues in comparison to at least one remaining variant.
- [00118] In some embodiments, (d) comprises identifying a variant which comprises only conservative non-anchor residues in comparison to at least 25%, at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% of the remaining variants.
- [00119] In some embodiments, (a) comprises aligning the sequences of said antigens.

- [00120] In some embodiments, (b) comprises comprises choosing a variant which comprises preferred primary anchor residues of said motif.
- [00121] In some embodiments, (b) comprises comprises choosing a variant which occurs with high frequency within said population.
- [00122] In some embodiments, (b) comprises ranking said variants by frequency of occurrence within said population.
- [00123] In some embodiments, (b) comprises choosing a variant which comprises preferred primary anchor residues of said motif and which occurs with high frequency within said population.
- [00124] In some embodiments, (b) comprises ranking said variants by frequency of occurrence within said population.
- [00125] In some embodiments, the identified variant comprises the fewest conserved anchor residues in comparison to each of the remaining variants.
- [00126] In some embodiments, the remaining variants comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 27, 28, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 220, 240, 260, 280, or 300 variants.
- [00127] In some embodiments, the infectious agent is selected from the group consisting of: HIV, HBV, HCV, HPV, Plasmodium falciparum, Influenza virus, and Dengue virus, Epstein-Barr virus, Mycobacterium tuberculosis, Chlamydia, Candida albicans, Cryptococcus neoformans, Coccidoides spp., Histoplasma spp., Aspergillus fumigatis, Plasmodium spp., Trypanosoma spp., Schistosoma spp., and Leishmania spp.
- [00128] In some embodiments, the infectious agent is selected from the group consisting of: HIV, HBV, HCV, HPV, *Plasmodium falciparum*, Influenza virus, and Dengue virus.
- [00129] In some embodiments, the infectious agent is HIV and the antigen is selected from the group consisting of: Gag, Env, Pol, Nef, Rev, Tat, Vif, Vpr, and Vpu.
- [00130] In some embodiments, the infectious agent is HBV and the antigen is selected from the group consisting of: Pol, Env, Core, and NS1/Env2.
- [00131] In some embodiments, the infectious agent is HCV and the antigen is selected from the group consisting of: Core, E1, E2, NS1, NS2, NS3, NS4, and NS5.
- [00132] In some embodiments, the infectious agent is HPV and the antigen is selected from the group consisting of: E1, E2, E3, E4, E5, E6, E7, L1, and L2.

- [00133] In some embodiments, the infectious agent is *Plasmodium falciparum* and the antigen is selected from the group consisting of: CSP, SSP2, EXP1, LSA1.
- [00134] In some embodiments, the selected variant and the at least one remaining variant comprise different primary anchor residues of the same motif or supermotif.
- [00135] In some embodiments, the motif or supermotif is selected from the group consisting of those in Tables 1-2.
- [00136] In some embodiments, the conserved non-anchor residues are at any of positions 3-7 of said variant.
- [00137] In some embodiments, the variant comprises only 1-3 conserved non-anchor residues compared to at least one remaining variant.
- [00138] In some embodiments, the variant comprises only 1-2 conserved non-anchor residues compared to at least one remaining variant.
- [00139] In some embodiments, the variant comprises only 1 conserved non-anchor residue compared to at least one remaining variant.
- [00140] In some embodiments, the infectious agent is HPV, and further wherein, the HPV infectious agent is selected from the group consisting of HPV strains 16, 18, 31, 33, 45, 52, 56, and 58.
- [00141] In some embodiments, the variants are a population of naturally occurring variants.
- [00142] Optional Alignment. Optionally, antigen sequences, either full-length or partial, may be aligned mannually or by computer. Convenient computer programs for aligning multiple sequences include Omiga, Oxford software, version 1.1.3, using ClustalW alignment, using an open gap penalty of 10.0, extend gap penalty of 0.05, and delay divergent sequences of 40.0 (See, e.g., Table 21); and BLASTP 2.2.5 (Nov-16-2002) (Altschul, S.F., et al., Nucleic Acids Res. 25:3389-3402 (1997)) using a cutoff = 3e-88 (to select human sequences) (see, e.g., Table 20). Alternatively, alignments may be obtained through publicly available sources such as published journal articles and published patent documents or as disclosed herein (see, e.g., Tables 10-22).
- [00143] HLA Class I Motifs Indicative of CTL Inducing Peptide Epitopes. A large fraction of HLA class I and class II molecules can be classified into a relatively few supertypes, each respective supertype characterized by largely overlapping peptide binding repertoires, and consensus structures of the main peptide binding pockets. Thus,

peptides of the present invention are preferably identified by the primary residues of any one of several HLA-specific amino acid motifs, or if the presence of the motif corresponds to the ability to bind several allele-specific HLA antigens, a supermotif (see, e.g., Tables 1-2). The preferred primary residues are indicated in bold, while the tolerated primary residues are indicated by italics.

- [00144] The primary anchor residues of the HLA class I peptide epitope supermotifs and motifs are summarized in Tables 1-2. Preferred primary anchors are shown in bold, while tolerated primary anchors are shown in italics. Primary and secondary anchor positions for HLA Class I are summarized in Table 3. Allele-specific HLA molecules that fall within the various HLA class I supertypes are listed in Table 4. In some cases, patterns of amino acid residues are present in both a motif and a supermotif. The relationship of a particular motif and any related supermotif is indicated in the description of the individual motifs.
- [00145] Thus, the peptide motifs and supermotifs described below, and summarized in Tables 1-2, provide guidance for the identification and use of peptide epitopes comprising primary anchor residues of motifs or supermotifs in accordance with the invention.
- [00146] Allele-specific HLA molecules that comprise HLA class I supertype families are listed in Table 4.
- [00147] HLA-A1 supermotif. The HLA-A1 supermotif is characterized by the presence in peptide ligands of a small (T or S) or hydrophobic (L, I, V, or M) primary anchor residue in position 2, and an aromatic (Y, F, or W) primary anchor residue at the C-terminal position of the epitope. The corresponding family of HLA molecules that bind to the A1 supermotif (i.e., the HLA-A1 supertype) is comprised of at least A*0101, A*2601, A*2602, A*2501, and A*3201 (see, e.g., DiBrino, M. et al., J. Immunol. 151:5930, 1993; DiBrino, M. et al., J. Immunol. 152:620, 1994; Kondo, A. et al., Immunogenetics 45:249, 1997). Other allele-specific HLA molecules predicted to be members of the A1 superfamily are shown in Table 4. Peptides binding to each of the individual HLA proteins can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the supermotif.
- [00148] HLA-A2 supermotif. Primary anchor specificities for allele-specific HLA-A2.1 molecules (see, e.g., Falk et al., Nature 351:290-296, 1991; Hunt et al., Science 255:1261-1263, 1992; Parker et al., J. Immunol. 149:3580-3587, 1992; Ruppert et al., Cell 74:929-937, 1993) and cross-reactive binding among HLA-A2 and -A28 molecules have been

- described. (See, e.g., Fruci et al., Human Immunol. 38:187-192, 1993; Tanigaki et al., Human Immunol. 39:155-162, 1994; Del Guercio et al., J. Immunol. 154:685-693, 1995; Kast et al., J. Immunol. 152:3904-3912, 1994 for reviews of relevant data.) These primary anchor residues define the HLA-A2 supermotif; which presence in peptide ligands corresponds to the ability to bind several different HLA-A2 and -A28 molecules. The HLA-A2 supermotif comprises peptide ligands with L, I, V, M, A, T, or Q as a primary anchor residue at position 2 and L, I, V, M, A, or T as a primary anchor residue at the C-terminal position of the epitope.
- [00149] The corresponding family of HLA molecules (i.e., the HLA-A2 supertype that binds these peptides) is comprised of at least: A*0201, A*0202, A*0203, A*0204, A*0205, A*0206, A*0207, A*0209, A*0214, A*6802, and A*6901. Other allele-specific HLA molecules predicted to be members of the A2 superfamily are shown in Table 4. As explained in detail below, binding to each of the individual allele-specific HLA molecules can be modulated by substitutions at the primary anchor and/or secondary anchor positions, preferably choosing respective residues specified for the supermotif.
- [00150] The motifs comprising the primary anchor residues V, A, T, or Q at position 2 and L, I, V, A, or T at the C-terminal position are those most particularly relevant to the invention claimed herein.
- [00151] HLA-A3 supermotif. The HLA-A3 supermotif is characterized by the presence in peptide ligands of A, L, I, V, M, S, or, T as a primary anchor at position 2, and a positively charged residue, R or K, at the C-terminal position of the epitope, e.g., in position 9 of 9-mers (see, e.g., Sidney et al., Hum. Immunol. 45:79, 1996). Exemplary members of the corresponding family of HLA molecules (the HLA-A3 supertype) that bind the A3 supermotif include at least A*0301, A*1101, A*3101, A*3301, and A*6801. Other allele-specific HLA molecules predicted to be members of the A3 supertype are shown in Table 4. As explained in detail below, peptide binding to each of the individual allele-specific HLA proteins can be modulated by substitutions of amino acids at the primary and/or secondary anchor positions of the peptide, preferably choosing respective residues specified for the supermotif.
- [00152] HLA-A24 supermotif. The HLA-A24 supermotif is characterized by the presence in peptide ligands of an aromatic (F, W, or Y) or hydrophobic aliphatic (L, I, V, M, or T) residue as a primary anchor in position 2, and Y, F, W, L, I, or M as primary anchor at the C-terminal position of the epitope (see, e.g., Sette and Sidney, Immunogenetics, in press,

1999). The corresponding family of HLA molecules that bind to the A24 supermotif (i.e., the A24 supertype) includes at least A*2402, A*3001, and A*2301. Other allele-specific HLA molecules predicted to be members of the A24 supertype are shown in Table 4. Peptide binding to each of the allele-specific HLA molecules can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the supermotif.

HLA-B7 supermotif. The HLA-B7 supermotif is characterized by peptides [00153] bearing proline in position 2 as a primary anchor, and a hydrophobic or aliphatic amino acid (L, I, V, M, A, F, W, or Y) as the primary anchor at the C-terminal position of the epitope. The corresponding family of HLA molecules that bind the B7 supermotif (i.e., the HLA-B7 supertype) is comprised of at least twenty six HLA-B proteins including: B*0702, B*0703, B*0704, B*0705, B*1508, B*3501, B*3502, B*3503, B*3504, B*3505, B*3506, B*3507, B*3508, B*5101, B*5102, B*5103, B*5104, B*5105, B*5301, B*5401, B*5501, B*5502, B*5601, B*5602, B*6701, and B*7801 (see, e.g., Sidney, et al., J. Immunol. 154:247, 1995; Barber, et al., Curr. Biol. 5:179, 1995; Hill, et al., Nature 360:434, 1992; Rammensee, et al., Immunogenetics 41:178, 1995 for reviews of relevant data). Other allele-specific HLA molecules predicted to be members of the B7 supertype are shown in Table 4. As explained in detail below, peptide binding to each of the individual allele-specific HLA proteins can be modulated by substitutions at the primary and/or secondary anchor positions of the peptide, preferably choosing respective residues specified for the supermotif.

in peptide ligands of a positively charged (R, H, or K) residue as a primary anchor at position 2, and a hydrophobic (F, Y, L, W, M, I, A, or V) residue as a primary anchor at the C-terminal position of the epitope (see, e.g., Sidney and Sette, Immunogenetics, in press, 1999). Exemplary members of the corresponding family of HLA molecules that bind to the B27 supermotif (i.e., the B27 supertype) include at least B*1401, B*1402, B*1509, B*2702, B*2703, B*2704, B*2705, B*2706, B*3801, B*3901, B*3902, and B*7301. Other allele-specific HLA molecules predicted to be members of the B27 supertype are shown in Table 4. Peptide binding to each of the allele-specific HLA molecules can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the supermotif.

- in peptide ligands of negatively charged (D or E) residues as a primary anchor in position 2, and hydrophobic residues (F, W, Y, L, I, M, V, or A) as a primary anchor at the C-terminal position of the epitope (see, e.g., Sidney et al., Immunol. Today 17:261, 1996). Exemplary members of the corresponding family of HLA molecules that bind to the B44 supermotif (i.e., the B44 supertype) include at least: B*1801, B*1802, B*3701, B*4001, B*4002, B*4006, B*4402, B*4403, and B*4006. Peptide binding to each of the allele-specific HLA molecules can be modulated by substitutions at primary and/or secondary anchor positions; preferably choosing respective residues specified for the supermotif.
- [00156] HLA-B58 supermotif. The HLA-B58 supermotif is characterized by the presence in peptide ligands of a small aliphatic residue (A, S, or T) as a primary anchor residue at position 2, and an aromatic or hydrophobic residue (F, W, Y, L, I, V, M, or A) as a primary anchor residue at the C-terminal position of the epitope (see, e.g., Sidney and Sette, Immunogenetics, in press, 1999 for reviews of relevant data). Exemplary members of the corresponding family of HLA molecules that bind to the B58 supermotif (i.e., the B58 supertype) include at least: B*1516, B*1517, B*5701, B*5702, and B*5801. Other allele-specific HLA molecules predicted to be members of the B58 supertype are shown in Table 4. Peptide binding to each of the allele-specific HLA molecules can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the supermotif.
- [00157] HLA-B62 supermotif. The HLA-B62 supermotif is characterized by the presence in peptide ligands of the polar aliphatic residue Q or a hydrophobic aliphatic residue (L, V, M, I, or P) as a primary anchor in position 2, and a hydrophobic residue (F, W, Y, M, I, V, L, or A) as a primary anchor at the C-terminal position of the epitope (see, e.g., Sidney and Sette, Immunogenetics, in press, 1999). Exemplary members of the corresponding family of HLA molecules that bind to the B62 supermotif (i.e., the B62 supertype) include at least: B*1501, B*1502, B*1513, and B5201. Other allele-specific HLA molecules predicted to be members of the B62 supertype are shown in Table 4. Peptide binding to each of the allele-specific HLA molecules can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the supermotif.
- [00158] HLA-A1 motif. The HLA-A1 motif is characterized by the presence in peptide ligands of T, S, or M as a primary anchor residue at position 2 and the presence of Y as a

primary anchor residue at the C-terminal position of the epitope. An alternative allele-specific A1 motif is characterized by a primary anchor residue at position 3 rather than position 2. This motif is characterized by the presence of D, E, A, or S as a primary anchor residue in position 3, and a Y as a primary anchor residue at the C-terminal position of the epitope (see, e.g., DiBrino et al., J. Immunol., 152:620, 1994; Kondo et al., Immunogenetics 45:249, 1997; and Kubo et al., J. Immunol. 152:3913, 1994 for reviews of relevant data). Peptide binding to HLA A1 can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the motif.

[00159] Those epitopes comprising T, S, or M at position 2 and Y at the C-terminal position are also HLA-A1 supermotif-bearing peptide epitopes, as these residues are a subset of the A1 supermotif primary anchors.

HLA-A*0201 motif. An HLA-A2*0201 motif was determined to be characterized [00160] by the presence in peptide ligands of L or M as a primary anchor residue in position 2, and L or V as a primary anchor residue at the C-terminal position of a 9-residue peptide (see, e.g., Falk et al., Nature 351:290-296, 1991) and was further found to comprise an I at position 2 and I or A at the C-terminal position of a nine amino acid peptide (see, e.g., Hunt et al., Science 255:1261-1263, March 6, 1992; Parker et al., J. Immunol. 149:3580-3587, 1992). The A*0201 allele-specific motif has also been defined by the present inventors to additionally comprise V, A, T, or Q as a primary anchor residue at position 2, and M or T as a primary anchor residue at the C-terminal position of the epitope (see, e.g., Kast et al., J. Immunol. 152:3904-3912, 1994). Thus, the HLA-A*0201 motif comprises peptide ligands with L, I, V, M, A, T, or Q as primary anchor residues at position 2 and L, I, V, M, A, or T as a primary anchor residue at the C-terminal position of the epitope. The preferred and tolerated residues that characterize the primary anchor positions of the HLA-A*0201 motif are identical to the residues describing the A2 supermotif. (For reviews of relevant data, see, e.g., Del Guercio et al., J. Immunol. 154:685-693, 1995; Ruppert et al., Cell 74:929-937, 1993; Sidney et al., Immunol. Today 17:261-266, 1996; Sette and Sidney, Curr. Opin. in Immunol. 10:478-482, 1998). Secondary anchor residues that characterize the A*0201 motif have additionally been defined (see, e.g., Ruppert et al., Cell 74:929-937, 1993). These are shown in Table 3. Peptide binding to HLA-A*0201 molecules can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the motif.

- [00161] HLA-A3 motif. The HLA-A3 motif is characterized by the presence in peptide ligands of L, M, V, I, S, A, T, F, C, G, or D as a primary anchor residue at position 2, and the presence of K, Y, R, H, F, or A as a primary anchor residue at the C-terminal position of the epitope (see, e.g., DiBrino et al., Proc. Natl. Acad. Sci USA 90:1508, 1993; and Kubo et al., J. Immunol. 152:3913-3924, 1994). Peptide binding to HLA-A3 can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the motif.
- [00162] The A3 supermotif primary anchor residues comprise a subset of the A3- and A11-allele specific motif primary anchor residues.
- [00163] HLA-A11 motif. The HLA-A11 motif is characterized by the presence in peptide ligands of V, T, M, L, I, S, A, G, N, C, D, or F as a primary anchor residue in position 2, and K, R, Y, or H as a primary anchor residue at the C-terminal position of the epitope (see, e.g., Zhang et al., Proc. Natl. Acad. Sci USA 90:2217-2221, 1993; and Kubo et al., J. Immunol. 152:3913-3924, 1994). Peptide binding to HLA-A11 can be modulated by substitutions at primary and/or secondary anchor positions, preferably choosing respective residues specified for the motif.
- [00164] There is extensive overlap between the A3 and A11 motif primary anchor specificities.
- [00165] HLA-A24 motif. The HLA-A24 motif is characterized by the presence in peptide ligands of Y, F, W, or M as a primary anchor residue in position 2, and F, L, I, or W as a primary anchor residue at the C-terminal position of the epitope (see, e.g., Kondo et al., J. Immunol. 155:4307-4312, 1995; and Kubo et al., J. Immunol. 152:3913-3924, 1994). Peptide binding to HLA-A24 molecules can be modulated by substitutions at primary and/or secondary anchor positions; preferably choosing respective residues specified for the motif.
- [00166] The primary anchor residues characterizing the A24 allele-specific motif comprise a subset of the A24 supermotif primary anchor residues.
- [00167] Computer or Manual Screening. Peptides bearing HLA Class I or Class II supermotifs or motifs may be identified by computer searches or manually, e.g., as follows. In utilizing computer screening to identify peptide epitopes, a protein sequence or translated sequence may be analyzed using software developed to search for motifs, for example the "FINDPATTERNS" program (Devereux, et al. Nucl. Acids Res. 12:387-395,

1984) or MotifSearch 1.4 software program (D. Brown, San Diego, CA) to identify potential peptide sequences containing appropriate HLA binding motifs. The identified peptides can be scored using customized polynomial algorithms to predict their capacity to bind specific HLA class I or class II alleles. As appreciated by one of ordinary skill in the art, a large array of computer programming software and hardware options are available in the relevant art which can be employed to implement the motifs in order to evaluate (e.g., without limitation, to identify epitopes, identify epitope concentration per peptide length, or to generate analogs) known or unknown peptide sequences.

- [00168] Translated antigen protein sequences may be analyzed using a text string search software program, e.g., MotifSearch 1.4 (D. Brown, San Diego) to identify potential peptide sequences containing appropriate HLA binding motifs; alternative programs are readily produced in accordance with information in the art in view of the motif/supermotif disclosure herein. Furthermore, such calculations can be made mentally.
- [00169] Identified supermotif or motif sequences may be scored using polynomial algorithms to predict their capacity to bind to specific HLA-Class I or Class II molecules. These polynomial algorithms take into account both extended and refined motifs (that is, to account for the impact of different amino acids at different positions), and are essentially based on the premise that the overall affinity (or ΔG) of peptide-HLA molecule interactions can be approximated as a linear polynomial function of the type:

"
$$\Delta G$$
" = $a_{1i} \times a_{2i} \times a_{3i} \dots \times a_{ni}$

where a_{ji} is a coefficient which represents the effect of the presence of a given amino acid (j) at a given position (i) along the sequence of a peptide of n amino acids. The crucial assumption of this method is that the effects at each position are essentially independent of each other (i.e., independent binding of individual side-chains). When residue j occurs at position i in the peptide, it is assumed to contribute a constant amount j_i to the free energy of binding of the peptide irrespective of the sequence of the rest of the peptide. This assumption is justified by studies from our laboratories that demonstrated that peptides are bound to MHC and recognized by T cells in essentially an extended conformation (data omitted herein).

[00170] The method of derivation of specific algorithm coefficients has been described in Gulukota et al., J. Mol. Biol. 267:1258-126, 1997; (see also Sidney et al., Human Immunol. 45:79-93, 1996; and Southwood et al., J. Immunol. 160:3363-3373, 1998). Briefly, for all i positions, anchor and non-anchor alike, the geometric mean of the average

relative binding (ARB) of all peptides carrying j is calculated relative to the remainder of the group, and used as the estimate of j_i . For Class II peptides, if multiple alignments are possible, only the highest scoring alignment is utilized, following an iterative procedure. To calculate an algorithm score of a given peptide in a test set, the ARB values corresponding to the sequence of the peptide are multiplied. If this product exceeds a chosen threshold, the peptide is predicted to bind. Appropriate thresholds are chosen as a function of the degree of stringency of prediction desired.

- of specific motifs, include the use of neural networks and molecular modeling programs (see, e.g., Milik et al., Nature Biotechnology 16:753, 1998; Altuvia et al., Hum. Immunol. 58:1, 1997; Altuvia et al, J. Mol. Biol. 249:244, 1995; Buus, S. Curr. Opin. Immunol. 11:209-213, 1999; Brusic, V. et al., Bioinformatics 14:121-130, 1998; Parker et al., J. Immunol. 152:163, 1993; Meister et al., Vaccine 13:581, 1995; Hammer et al., J. Exp. Med. 180:2353, 1994; Sturniolo et al., Nature Biotechnol. 17:555 1999).
- [00172] Conserved, Semi-conserved, and Non-conserved Non-anchor Residues. The determination of non-anchor residues as being conserved (conservative) or semi-conserved (semi-conservative) or non-conserved (non-conservative) in comparison to the non-anchor poitions of from one to all of the remaining variant(s) is defined by as follows, the results of which are summarized in Table 5.
- [00173] Table 5 shows the similarity assignments between any given amino acid pair so that a given amino acid substitution could be characterized as being a (conservative) or semi-conserved (semi-conservative) or non-conserved (non-conservative) residue.
- [00174] The degree of similarity between amino acid pairs was quantified by averaging, for each amino acid pair, the rank coefficient scores for PAM250, hydrophobicity, and side chain volume as described below. Based on the average values of these composite rankings, Table 5 shows each pair to be conserved, semi-conserved or non-conserved.
- [00175] The Dayhoff PAM250 score (Dayhoff, M.O., et al., Atlas of Protein Sequence and Structure, Vol. 5, suppl.3. (1978) M.O. Dayhoff, ed. National Biomedical Research Foundation, Washington DC, p. 345; Creighton, T.E., Proteins: structures and molecular properties (1993) (2nd edition) W.H. Freeman and Company, NY; is a commonly utilized protein alignment scoring matrix which measures the percentage of acceptable point

mutations (PAM) within a defined time frame. The frequencies of these mutations are different from what would be expected from the probability of random mutations, and presumably reflect a bias due to the degree of physical and chemical similarity of the amino acid pair involved in the substitution. To obtain a score of amino acid similarity that could be standardized with other measures of similarity, the PAM250 scores were converted to a rank value, where 1 indicates the highest probability of being an accepted mutation.

- [00176] The most commonly utilized scales to represent the relative hydrophobicity of the 20 naturally occurring amino acids (Cornette, J., et al., J. Mol. Biol. (1987) 195:659) are those developed on the basis of experimental data by Kyte and Doolittle (Kyte, J. and R.F. Doolittle, J. Mol. Biol. (1982) 157:105), and by Fauchere and Pliska (Fauchere, J. and V. Pliska, Eur. J. Med. Chem. (1983) 18:369). The Kyte/Doolittle scale measures the H₂O/organic solvent partition of individual amino acids. Because it considers the position of amino acids in folded proteins, it may most accurately reflect native hydrophobicity in the context of proteins. The Fauchere/Pliska scale measures the octanol/H₂O partitioning of N-acetyl amino acid amides, and most accurately reflects hydrophobicity in the context of denatured proteins and/or small synthetic peptides. To obtain scores for hydrophobicity, each amino acid residue was ranked on both the Kyte/Doolittle and Fauchere/Pliska hydrophobicity scales. An average rank between the two scales was calculated and the average difference in hydrophobicity for each pair was calculated.
- [00177] Finally, for calculating amino acid side-chain volume, the partial volume in solution obtained by noting the increase in volume of water after adding either one molecule or one gram of amino acid residue was considered (Zamyatnin, A.A., Ann. Rev. Biophys. Bioeng. (1984) 13:145; Zamyatnin, A.A., Prog. Biophys. Mol. Biol. (1972) 24:107). The absolute difference in the partial volume of each possible pairing of the 20 naturally occurring amino acids was calculated and ranked, where 1 indicated residues with the most similar volumes, and 20 the most dissimilar.
- [00178] Thus, by consulting Table 5, one can determine whether a residue in a variant is considered to be conserved, semi-conserved, or non-conserved in comparison to a residue in another variant(s). The residue of the parent variant (randomly or otherwise chosen variant) is shown across the top of Table 5, and the residue of the variant(s) it is compared with is shown below the parent residue.

[00179] As shown in Table 5, each of the amino acids shown across the top of the table bears a numerically defined relationship to the remaining 19 genetically encoded amino acids. The lower the index, the higher the conservation; the same amino acid will have a similarity assignment of 1.0; maximally different amino acids will have similarity assignments approaching 20. Using the method set forth above, amino acids which are not gene-encoded can also be assigned similarity indices and can be classified with respect to any natively occurring amino acid as conserved (conservative) or semi-conserved (semi-conservative) or non-conserved (non-conservative).

Variant Peptide Epitopes

- [00180] In some embodiments, the invention is directed to an isolated peptide comprising or consisting of a variant. In some embodiments, the invention is directed to an isolated polynucleotide encoding such a peptide.
- In particular, the variants of the invention are all class I binding peptides, i.e., CTL peptides. Variants of the invention are those set forth in Tables 6-9 and Figures 1A-4 (SEQ ID Nos: 1,2,9-13, 15,16,18-26, 56-60, 69, 71, 72, 74,77-89, 91-96,99-101, 103, 105, 108, 109, 112-117, 119, 120, 123-127, 129, 130, 132, 133, 136-142, 145-152, 154-158, 160-165, 167, 168, 172-175, 177-179, 181, 182, 184-186, 188, 189, 191-212, 222-237, 262-277). Variants of the invention may be referred to herein as "variants" and "variant peptide epitopes" or referred to by Table or referred to by SEQ ID NO. Other peptide epitopes are referred to herein as CTL epitopes or CTL peptides and HTL epitopes or HTL peptides.
- [00182] Peptides and Polynucleotides. In some embodiments, the invention is directed to an isolated peptide comprising or consisting of a variant, wherein the variant consists of a sequence selected from those in Tables 6-9 and Figures 1A-4 (SEQ ID Nos:[__]] 1.2, 9-13, 15,16,18-26, 56-60, 69, 71, 72, 74,77-89, 91-96,99-101, 103, 105, 108, 109, 112-117, 119, 120, 123-127, 129, 130, 132, 133, 136-142, 145-152, 154-158, 160-165, 167, 168, 172-175, 177-179, 181, 182, 184-186, 188, 189, 191-212, 222-237, 262-277).
- [00183] Peptides of the invention may be fusion proteins of variant(s) to CTL epitope(s), and/or HTL epitope(s), and/or linker(s), and/or spacer(s), and/or carrier(s), and/or additional amino acid(s), and/or may comprise or consist of homopolymers of a variant or heteropolymers of more than one variant, as is described in detail below.
- [00184] Peptides which comprise a variant of the invention may comprise or consist of a fragment of an antigen ("fragment" or "antigenic fragment"), wherein the fragment comprises a variant. The fragment may be a portion of any antigen of an infectious agent, e.g., the sequences in Tables 11-

22 (SEQ ID Nos:[[__]] 302-1755, respectively). The variant of the invention may be within the fragment or may be linked, directly or indirectly, to the fragment.

- [00185] The fragment may comprise or consist of a region of a native antigen that contains a high concentration of class I and/or class II epitopes, preferably it contains the greatest number of epitopes per amino acid length. Such epitopes can be present in a frame-shifted manner, e.g. a 10 amino acid long peptide could contain two 9 amino acid long epitopes and one 10 amino acid long epitope.
- [00186] The fragment may be less than or equal to 600 amino acids, less than or equal to 500 amino acids, less than or equal to 400 amino acids, less than or equal to 250 amino acids, less than or equal to 100 amino acids, less than or equal to 85 amino acids, less than or equal to 75 amino acids, less than or equal to 65 amino acids, or less than or equal to 50 amino acids in length. In certain embodiments, a fragment is less than 101 amino acids in length, in any increment down to 5 amino acids in length. For example, the fragment may be 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 amino acids in length. Fragments of full length antigens may be fragments from about residue 1-20, 21-40, 41-60, 61-80, 81-100, 101-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-680, 681-700, 701-720, 721-740, 741-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981 to the C-terminus of the antigen.
- [00187] Peptides which comprise a variant of the invention may be a fusion protein comprising one or more amino acid residues in addition to the variant or fragment. Fusion proteins include homopolymers and heteropolymers, as described below.
- [00188] In some embodiments, the peptide comprises or consists of multiple variants, e.g., 2, 3, 4, 5, 6, 7, 8, or 9 variants of the invention. In some embodiments, the peptide comprises at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 variants of the invention.
- [00189] The peptide may also be a homopolymer of one variant or the peptide may be a heteropolymer which contains at least two different variants. Polymers have the advantage of increased probability for immunological reaction and, where different variants are used to make up the polymer, the ability to induce antibodies and/or T cells that react with different antigenic determinants of the antigen(s) targeted for an immune response.
- [00190] A homopolymer may comprise 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60, 65,

70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, or 150 copies of the same variant.

- A heteropolymer may comprise one or more copies of an individual variant and one or more copies of one or more different variants of the invention. The variants that form a heteropolymer may all be from the same antigen, e.g., may be from any of those in Tables 11-22 (SEQ ID NOS:[_]] 302-1755) or other antigens herein or known in the art, or may be from different antigens, preferably from infectious agents. Combinations of variants that may form a heteropolymer include, for example, Gag 545 variants EPLTSLKSLF (SEQ ID NO:[_]] 1) and YPLASLKSLF (SEQ ID NO:[_]] 2), or combinations of peptides from different tables in Tables 6-9 (SEQ ID NOS: 1,2, 9-13, 15,16,18-26, 56-60, 69, 71, 72, 74,77-89, 91-96,99-101, 103, 105, 108, 109, 112-117, 119, 120, 123-127, 129, 130, 132, 133, 136-142, 145-152, 154-158, 160-165, 167, 168, 172-175, 177-179, 181, 182, 184-186, 188, 189, 191-212, 222-237, 262-277) and/or Figures 1A-4 (Figure 1A, SEQ ID NOS: 1756-1775; Figure 1B, SEQ ID NOS: 1776-1796; Figure 1C, SEQ ID NOS: 1797-1820; Figure 1D, SEQ ID NOS: 1821-1851; Figure 1E, SEQ ID NOS: 1852-1861; and Figure 4, SEQ ID NOS: 1919-1933) or those combinations in Tables 23-28 (SEQ ID NOS: 1934 1946). Heteropolymers may contain multiple copies of one or more variants.
- [00192] Thus, peptides of the invention such as heteropolymers may comprise a first variant and at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 other (different) variants.
- [00193] In some embodiments, the peptide comprising a variant may also comprise a number of CTL and/or HTL epitopes, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 CTL and/or HTL epitopes.
- [00194] The CTL and/or HTL epitope and the variant of the invention may be from the same antigen of an infectious agent or from different antigens. Thus, for example, if the variant is from HIV pol, the CTL peptide and/or HTL peptide may also be from HIV pol. Alternatively, if the variant is from HIV pol, the CTL peptide and/or HTL peptide may be from another antigen such as HIV env or HIV vpr. As another example, if the variant is from HBV E6, the CTL peptide and/or HTL peptide may be from HBV E7. The CTL and/or HTL epitope and the variant of the invention may be from the same infectious agent or different infectious agents. Thus, for example, the variant may be from HIV, and the CTL and/or HTL epitope may be from HIV or may be from another infectious agent sush such as HBV, HCV, HPV, or *Plasmodium falciparum*.
- [00195] The CTL peptide and/or HTL peptide may be from other antigens including hepatitis B core and surface antigens (HBVc, HBVs), hepatitis C antigens, Epstein-Barr virus antigens, human immunodeficiency virus (HIV) antigens and human papilloma virus (HPV) antigens (in particular

anitgens from HPV-16, HPV-18, HPV-31, HPV-33, HPV-45, HPV-52, HPV-56 and HPV-58, Mycobacterium tuberculosis and Chlamydia. Examples of suitable fungal antigens include those derived from Candida albicans, Cryptococcus neoformans, Coccidoides spp., Histoplasma spp, and Aspergillus fumigatis. Examples of suitable protozoan parasitic antigens include those derived from Plasmodium spp., including P. falciparum, Trypanosoma spp., Schistosoma spp., Leishmania spp and the like.

- Alternatively, the CTL peptide and/or HTL peptide may be from tumor-associated antigens such as but not limited to, melanoma antigens MAGE-1, MAGE-2, MAGE-3, MAGE-11, MAGE-A10, as well as BAGE, GAGE, RAGE, MAGE-C1, LAGE-1, CAG-3, DAM, MUC1, MUC2, MUC18, NY-ESO-1, MUM-1, CDK4, BRCA2, NY-LU-1, NY-LU-7, NY-LU-12, CASP8, RAS, KIAA-2-5, SCCs, p53, p73, CEA, HER2/neu, Melan-A, gp100, tyrosinase, TRP2, gp75/TRP1, kallikrein, prostate-specific membrane antigen (PSM), prostatic acid phosphatase (PAP), prostate-specific antigen (PSA), PT1-1, ∃-catenin, PRAME, Telomerase, FAK, cyclin D1 protein, NOEY2, EGF-R, SART-1, CAPB, HPVE7, p15, Folate receptor CDC27, PAGE-1, and PAGE-4.
- [00197] Examples of CTL peptides and HTL peptides are disclosed in WO 01/42270, published 14 June 2001; WO 01/41788, published 14 June 2001; WO 01/42270, published 14 June 2001; WO 01/45728, published 28 June 2001; and WO 01/41787, published 14 June 2001.
- [00198] The HTL peptide may comprise a "loosely HLA-restricted" or "promiscuous" sequence. Examples of amino acid sequences that are promiscuous include sequences from antigens such as tetanus toxoid at positions 830-843 (QYIKANSKFIGITE; SEQ ID NO: [[627]] 3), Plasmodium falciparum CS protein at positions 378-398 (DIEKKIAKMEKASSVFNVVNS; SEQ ID NO: [[628]] 5), and Streptococcus 18kD protein at positions 116-131 (GAVDSILGGVATYGAA; SEQ ID NO: [[629]] 5). Other examples include peptides bearing a DR 1-4-7 supermotif, or either of the DR3 motifs.
- [00199] The HTL peptide may comprise a synthetic peptide such as a Pan-DR-binding epitope (e.g., a PADRE® peptide, Epimmune Inc., San Diego, CA, described, for example, in U.S. Patent Number 5,736,142), for example, having the formula aKXVAAZTLKAAa, where "X" is either cyclohexylalanine, phenylalanine, or tyrosine; "Z" is either tryptophan, tyrosine, histidine or asparagine; and "a" is either D-alanine or L-alanine (SEQ ID NO: 746). Certain pan-DR binding epitopes comprise all "L" natural amino acids; these molecules can be provided as peptides or in the form of nucleic acids that encode the peptide. See also, U.S. Patent Nos. 5,679,640 and 6,413,935.

- [00200] The peptide comprising a variant may comprise additional amino acid(s). Such additional amino acids may be Ala, Arg, Asn, Asp, Cys, Gln, Gly, Glu, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Tyr, Trp, Val, amino acid mimetics, and other unnatural amino acids such as those described below. Additional amino acids may provide for ease of linking peptides one to another, for linking variants to one another, for linking variants to CTL and/or HTL epitopes, for coupling to a carrier support or larger peptide, for modifying the physical or chemical properties of the peptide or oligopeptide, or the like. Amino acids such as Ala, Arg, Asn, Asp, Cys, Gln, Gly, Glu, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Tyr, Trp, or Val, or the like, can be introduced at the C- and/or N-terminus of the peptide and/or can be introduced internally.
- [00201] The peptide comprising a variant may comprise an amino acid spacer(s), which may be joined to the variants, CTL epitopes, HTL epitopes, carriers, etc. within a peptide or may be joined to the peptide at the N-and/or C-terminus. Thus, spacers may be at the N-terminus or C-terminus of peptide, or may be internal such that they link or join variants, CTL epitopes, HTL epitopes, carriers, additional amino acids, and/or antigenic fragments one to the other.
- [00202] The spacer is typically comprised of one or more relatively small, neutral molecules, such as amino acids or amino acid mimetics, which are substantially uncharged under physiological conditions. The spacers are typically selected from, e.g., Ala, Gly, or other neutral spacers of nonpolar amino acids or neutral polar amino acids. It will be understood that the optionally present spacer may be composed of the same residues or may be composed of one or more different residues and thus may be a homo- or heterooligomer of spacer residues. Thus, the spacer may contain more than one Ala residue (poly-alanine) or more than one Gly residue (poly-glycine), or may contain both Ala and Gly residues. Gly, Gly-Gly-, Ser, Ser-Ser-, e.g., Gly-Ser-, Ser-Gly-, etc. When present, the spacer will usually be at least one or two residues, more usually three to six residues and sometimes 10 or more residues, e.g., 3, 4, 5, 6, 7, 8, 9, or 10, or even more residues. (Livingston, B.D. et al. Vaccine 19:4652-4660 (2000)).
- [00203] Peptides comprising a variant may comprise carrier(s) such as those well known in the art, e.g., thyroglobulin, albumins such as human serum albumin, tetanus toxoid, polyamino acids such as poly L-lysine, poly L-glutamic acid, influenza virus proteins, hepatitis B virus core protein, and the like. (See Table 29).

[00204] In addition, the peptide comprising or consisting of a variant may be modified by terminal-NH₂ acylation, e.g., by alkanoyl (C₁-C₂₀) or thioglycolyl acetylation, terminal-carboxyl amidation, e.g., ammonia, methylamine, etc. In some instances these modifications may provide sites for linking to a support or other molecule.

[00205] The peptides in accordance with the invention can contain modifications such as but not limited to glycosylation, side chain oxidation, biotinylation, phosphorylation, addition of a surface active material, e.g. a lipid, or can be chemically modified, e.g., acetylation, etc. Moreover, bonds in the peptide can be other than peptide bonds, e.g., covalent bonds, ester or ether bonds, disulfide bonds, hydrogen bonds, ionic bonds, etc.

[00206] Peptides of the present invention may contain substitutions to modify a physical property (e.g., stability or solubility) of the resulting peptide. For example, peptides may be modified by the substitution of a cysteine (C) with α-amino butyric acid ("B"). Due to its chemical nature, cysteine has the propensity to form disulfide bridges and sufficiently alter the peptide structurally so as to reduce binding capacity. Substituting α-amino butyric acid for C not only alleviates this problem, but actually improves binding and crossbinding capability in certain instances. Substitution of cysteine with α-amino butyric acid may occur at any residue of a peptide, e.g., at either anchor or non-anchor positions of a variant within a peptide, or at other positions of a peptide.

[00207] The peptides comprising a variant can comprise amino acid mimetics or unnatural amino acids, e.g. D- or L-naphylalanine; D- or L-phenylglycine; D- or L-2-thieneylalanine; D- or L-1, -2, 3, or 4-pyreneylalanine; D- or L-3 thieneylalanine; D- or L-(2-pyridinyl)alanine; D- or L-(3-pyridinyl)-alanine; D- or L-(2-pyrazinyl)-alanine; D- or L-(4-isopropyl)phenylglycine; D-(trifluoromethyl)-phenylglycine; D-(trifluoromethyl)-phenylalanine; D-pfluorophenylalanine; Dor L-p-biphenylphenylalanine; Dor methoxybiphenylalanine; D- or L-2-indole(alkyl)alanines; and, Dalkylalanines, where the alkyl group can be a substituted or unsubstituted methyl, ethyl, propyl, hexyl, butyl, pentyl, isopropyl, iso-butyl, sec-isotyl, iso-pentyl, or a non-acidic Aromatic rings of a non-natural amino acid include, e.g., thiazolyl, amino acids. thiophenyl, pyrazolyl, benzimidazolyl, naphthyl, furanyl, pyrrolyl, and pyridyl aromatic rings. Modified peptides that have various amino acid mimetics or unnatural amino acids are particularly useful, as they tend to manifest increased stability in vivo. Such peptides may also possess improved shelf-life or manufacturing properties.

Peptide stability can be assayed in a number of ways. For instance, peptidases and various biological media, such as human plasma and serum, have been used to test stability. See, e.g., Verhoef, et al., Eur. J. Drug Metab. Pharmacokinetics 11:291 (1986). Half-life of the peptides of the present invention is conveniently determined using a 25% human serum (v/v) assay. The protocol is generally as follows: Pooled human serum (Type AB, non-heat inactivated) is delipidated by centrifugation before use. The serum is then diluted to 25% with RPMI-1640 or another suitable tissue culture medium. At predetermined time intervals, a small amount of reaction solution is removed and added to either 6% aqueous trichloroacetic acid (TCA) or ethanol. The cloudy reaction sample is cooled (4°C) for 15 minutes and then spun to pellet the precipitated serum proteins. The presence of the peptides is then determined by reversed-phase HPLC using stability-specific chromatography conditions.

[00209] As indicated above, the peptides in accordance with the invention can be a variety of lengths, and either in their neutral (uncharged) forms or in forms which are salts. The peptides in accordance with the invention can contain modifications such as glycosylation, side chain oxidation, or phosphorylation, generally subject to the condition that modifications do not destroy the biological activity of the peptides.

[00210] The peptides of the invention may be lyophylized, or may be in crystal form.

When possible, it may be desirable to optimize HLA class I binding epitopes of the invention to a length of about 8 to about 13 amino acid residues, for example, 8, 9, 10, 11, 12 or 13, preferably 8 to 11 or 9 to 10. It is to be appreciated that one or more epitopes in this size range can be comprised by a longer peptide (see the Definition Section for the term "epitope" for further discussion of peptide length). HLA class II binding epitopes are preferably optimized to a length of about 6 to about 30 amino acids in length, e.g., 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, preferably to between about 13 and about 20 residues, e.g., 13, 14, 15, 16, 17, 18, 19 or 20. Preferably, the epitopes are commensurate in size with endogenously processed pathogenderived peptides or tumor cell peptides that are bound to the relevant HLA molecules. The identification and preparation of peptides of various lengths can be carried out using the techniques described herein.

- [00212] Peptides in accordance with the invention can be prepared synthetically, by recombinant DNA technology or chemical synthesis, or can be isolated from natural sources such as native tumors or pathogenic organisms. Epitopes may be synthesized individually or joined directly or indirectly in a peptide. Although the peptide will preferably be substantially free of other naturally occurring host cell proteins and fragments thereof, in some embodiments the peptides may be synthetically conjugated to be joined to native fragments or particles.
- [00213] The peptides of the invention can be prepared in a wide variety of ways. For relatively short sizes, the peptides can be synthesized in solution or on a solid support in accordance with conventional techniques. Various automatic synthesizers are commercially available and can be used in accordance with known protocols. (See, for example, Stewart & Young, SOLID PHASE PEPTIDE SYNTHESIS, 2D. ED., Pierce Chemical Co., 1984). Further, individual peptides can be joined using chemical ligation to produce larger peptides that are still within the bounds of the invention.
- [00214] Alternatively, recombinant DNA technology can be employed wherein a nucleotide sequence which encodes a peptide inserted into an expression vector, transformed or transfected into an appropriate host cell and cultivated under conditions suitable for expression. These procedures are generally known in the art, as described generally in Sambrook *et al.*, Molecular Cloning, a Laboratory Manual, Cold Spring Harbor Press, Cold Spring Harbor, New York (1989). Thus, recombinant peptides, which comprise or consist of one or more epitopes of the invention, can be used to present the appropriate T cell epitope.
- [00215] Polynucleotides encoding each of the peptides above are also part of the invention. As appreciated by one of ordinary skill in the art, various nucleic acids will encode the same peptide due to the redundancy of the genetic code. Each of these nucleic acids falls within the scope of the present invention. This embodiment of the invention comprises DNA and RNA, and in certain embodiments a combination of DNA and RNA. It is to be appreciated that any polynucleotide that encodes a peptide in accordance with the invention falls within the scope of this invention.
- [00216] The polynucleotides encoding peptides contemplated herein can be synthesized by chemical techniques, for example, the phosphotriester method of Matteucci, et al., J. Am. Chem. Soc. 103:3185 (1981). Polynucleotides encoding peptides comprising or consisting

of a variant can be made simply by substituting the appropriate and desired nucleic acid base(s) for those that encode a related (e.g., analogous) epitope.

- [00217] The polynucleotide, e.g. minigene (see below), may be produced by assembling oligonucleotides that encode the plus and minus strands of the polynucleotide, e.g. minigene. Overlapping oligonucleotides (15-100 bases long) may be synthesized, phosphorylated, purified and annealed under appropriate conditions using well known techniques. The ends of the oligonucleotides can be joined, for example, using T4 DNA ligase. A polynucleotide, e.g. minigene, encoding the peptide of the invention, can be cloned into a desired vector such as an expression vector. The coding sequence can then be provided with appropriate linkers and ligated into expression vectors commonly available in the art, and the vectors used to transform suitable hosts to produce the desired peptide such as a fusion protein.
- [00218] A large number of such vectors and suitable host systems are known to those of skill in the art, and are commercially available. The following vectors are provided by way of example. Bacterial: pQE70, pQE60, pQE-9 (Qiagen), pBS, pD10, phagescript, psiX174, pBluescript SK, pbsks, pNH8A, pNH16a, pNH18A, pNH46A (Stratagene); ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia); pCR (Invitrogen). Eukaryotic: pWLNEO, pSV2CAT, pOG44, pXT1, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia); p75.6 (valentis); pCEP (Invitrogen); pCEI (Epimmune). However, any other plasmid or vector can be used as long as it is replicable and viable in the host.
- [00219] As representative examples of appropriate hosts, there can be mentioned: bacterial cells, such as *E. coli, Bacillus subtilis, Salmonella typhimurium* and various species within the genera Pseudomonas, Streptomyces, and Staphylococcus; fungal cells, such as yeast; insect cells such as Drosophila and Sf9; animal cells such as COS-7 lines of monkey kidney fibroblasts, described by Gluzman, *Cell 23*:175 (1981), and other cell lines capable of expressing a compatible vector, for example, the C127, 3T3, CHO, HeLa and BHK cell lines or Bowes melanoma; plant cells, etc. The selection of an appropriate host is deemed to be within the scope of those skilled in the art from the teachings herein.
- [00220] Thus, the present invention is also directed to vectors, preferably expression vectors useful for the production of the peptides of the present invention, and to host cells comprising such vectors.

- With the vectors of this invention which can be, for example, a cloning vector or an expression vector. The vector can be, for example, in the form of a plasmid, a viral particle, a phage, etc. The engineered host cells can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the polynucletides. The culture conditions, such as temperature, pH and the like, are those previously used with the host cell selected for expression, and will be apparent to the ordinarily skilled artisan.
- [00222] For expression of the peptides, the coding sequence will be provided with operably linked start and stop codons, promoter and terminator regions and usually a replication system to provide an expression vector for expression in the desired cellular host. For example, promoter sequences compatible with bacterial hosts are provided in plasmids containing convenient restriction sites for insertion of the desired coding sequence. The resulting expression vectors are transformed into suitable bacterial hosts.
- [00223] Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, e.g., the ampicillin resistance gene of E. coli and S. cerevisiae TRP1 gene, and a promoter derived from a highly-expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), ∀-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an N-terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product.
- [00224] Yeast, insect or mammalian cell hosts may also be used, employing suitable vectors and control sequences. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts, described by Gluzman, *Cell 23*:175 (1981), and other cell lines capable of expressing a compatible vector, for example, the C127, 3T3, CHO, HeLa and BHK cell lines. Mammalian expression vectors will comprise an origin of replication, a suitable promoter and enhancer, and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional

termination sequences, and 5' flanking nontranscribed sequences. Such promoters may also be derived from viral sources, such as, e.g., human cytomegalovirus (CMV-IE promoter) or herpes simplex virus type-1 (HSV TK promoter). Nucleic acid sequences derived from the SV40 splice, and polyadenylation sites can be used to provide the required nontranscribed genetic elements.

- [00225] Polynucleotides encoding peptides of the invention may also comprise a ubiquitination signal sequence, and/or a targeting sequence such as an endoplasmic reticulum (ER) signal sequence to facilitate movement of the resulting peptide into the endoplasmic reticulum.
- [00226] Polynucleotides of the invention, e.g., minigenes, may be expressed in human cells. A human codon usage table can be used to guide the codon choice for each amino acid. Such polynucleotides preferably comprise spacer amino acid residues between variants, such as those described above, or may comprise naturally-occurring flanking sequences adjacent to the variants (and/or CTL and HTL epitopes).
- [00227] The peptides of the invention can also be expressed by viral or bacterial vectors. Examples of expression vectors include attenuated viral hosts, such as vaccinia or fowlpox. As an example of this approach, vaccinia virus is used as a vector to express nucleotide sequences that encode the peptides of the invention. Vaccinia vectors and methods useful in immunization protocols are described in, e.g., U.S. Patent No. 4,722,848. Another vector is BCG (Bacille Calmette Guerin). BCG vectors are described in Stover et al., Nature 351:456-460 (1991). A wide variety of other vectors useful for therapeutic administration or immunization of the polypeptides of the invention, e.g. adeno and adeno-associated virus vectors, retroviral vectors, Salmonella typhi vectors, detoxified anthrax toxin vectors, and the like, will be apparent to those skilled in the art from the description herein. A preferred vector is Modified Vaccinia Ankara (MVA) (e.g., Bavarian Noridic (MVA-BN)).
- [00228] Standard regulatory sequences well known to those of skill in the art are preferably included in the vector to ensure expression in the human target cells. Several vector elements are desirable: a promoter with a downstream cloning site for polynucleotide, e.g., minigene insertion; a polyadenylation signal for efficient transcription termination; an E. coli origin of replication; and an E. coli selectable marker (e.g. ampicillin or kanamycin resistance). Numerous promoters can be used for this purpose, e.g., the human

cytomegalovirus (hCMV) promoter. See, e.g., U.S. Patent Nos. 5,580,859 and 5,589,466 for other suitable promoter sequences. A preferred promoter is the CMV-IE promoter.

- [00229] Polynucleotides, e.g. minigenes, may comprise one or more synthetic or naturallyoccurring introns in the transcribed region. The inclusion of mRNA stabilization sequences and sequences for replication in mammalian cells may also be considered for increasing polynucleotide, e.g. minigene, expression.
- [00230] In addition, the polynucleotide, e.g. minigene, may comprise immunostimulatory sequences (ISSs or CpGs). These sequences may be included in the vector, outside the polynucleotide (e.g. minigene) coding sequence to enhance immunogenicity.
- [00231] In some embodiments, a bi-cistronic expression vector which allows production of both the polynucleotide- (e.g. minigene-) encoded peptides of the invention and a second protein (e.g., one that modulates immunogenicity) can be used. Examples of proteins or polypeptides that, if co-expressed with peptides of the invention, can enhance an immune response include cytokines (e.g., IL-2, IL-12, GM-CSF), cytokine-inducing molecules (e.g., LeIF), costimulatory molecules, or pan-DR binding proteins (PADRE® molecules, Epimmune, San Diego, CA). Helper T cell (HTL) epitopes such as PADRE® molecules can be joined to intracellular targeting signals and expressed separately from expressed peptides of the invention. Specifically decreasing the immune response by co-expression of immunosuppressive molecules (e.g. TGF-β) may be beneficial in certain diseases.
- [00232] Once an expression vector is selected, the polynucleotide, e.g. minigene, is cloned into the polylinker region downstream of the promoter. This plasmid is transformed into an appropriate bacterial strain, and DNA is prepared using standard techniques. The orientation and DNA sequence of the polynucleotide, e.g. minigene, as well as all other elements included in the vector, are confirmed using restriction mapping, DNA sequence analysis, and/or PCR analysis. Bacterial cells harboring the correct plasmid can be stored as cell banks.
- [00233] Therapeutic/prophylactic quantities of DNA can be produced for example, by fermentation in *E. coli*, followed by purification. Aliquots from the working cell bank are used to inoculate growth medium, and are grown to saturation in shaker flasks or a bioreactor according to well known techniques. Plasmid DNA is purified using standard bioseparation technologies such as solid phase anion-exchange resins available, *e.g.*, from QIAGEN, Inc. (Valencia, California). If required, supercoiled DNA can be isolated from the open circular and linear forms using gel electrophoresis or other methods.

Purified polynucleotides, e.g. minigenes, can be prepared for injection using a [00234] The simplest of these is reconstitution of lyophilized variety of formulations. polynucleotide, e.g. DNA, in sterile phosphate-buffer saline (PBS). This approach, known as "naked DNA," is currently being used for intramuscular (IM) administration in clinical trials. To maximize the immunotherapeutic effects of polynucleotide vaccines, alternative methods of formulating purified plasmid DNA may be used. A variety of such methods have been described, and new techniques may become available. Cationic lipids, glycolipids, and fusogenic liposomes can also be used in the formulation (see, e.g., WO 93/24640; Mannino & Gould-Fogerite, BioTechniques 6(7): 682 (1988); U.S. Patent No. 5,279,833; WO 91/06309; and Felgner, et al., Proc. Nat'l Acad. Sci. USA 84:7413 (1987). In addition, peptides and compounds referred to collectively as protective, interactive, non-condensing compounds (PINC) can also be complexed to purified plasmid DNA to influence variables such as stability, intramuscular dispersion, or trafficking to specific organs or cell types.

[00235] Known methods in the art can be used to enhance delivery and uptake of a polynucleotide *in vivo*. For example, the polynucleotide can be complexed to polyvinylpyrrolidone (PVP), to prolong the localized bioavailability of the polynucleotide, thereby enhancing uptake of the polynucleotide by the organisum (*see e.g.*, U.S. Patent No. 6,040,295; EP 0 465 529; WO 98/17814). PVP is a polyamide that is known to form complexes with a wide variety of substances, and is chemically and physiologically inert.

[00236] Target cell sensitization can be used as a functional assay of the expression and HLA class I presentation of polynucleotide- (e.g. minigene-) encoded peptides. For example, the polynucleotide, e.g. plasmid DNA, is introduced into a mammalian cell line that is a suitable target for standard CTL chromium release assays. The transfection method used will be dependent on the final formulation. For example, electroporation can be used for "naked" DNA, whereas cationic lipids or PVP-formulated DNA allow direct *in vitro* transfection. A plasmid expressing green fluorescent protein (GFP) can be cotransfected to allow enrichment of transfected cells using fluorescence activated cell sorting (FACS). The transfected cells are then chromium-51 (51Cr) labeled and used as targets for epitope-specific CTLs. Cytolysis of the target cells, detected by 51Cr release, indicates both production and HLA presentation of, polynucleotide-, e.g. minigene-, encoded variants of the invention, or peptides comprising them. Expression of HTL epitopes may be evaluated in an analogous manner using assays to assess HTL activity.

[00237] In vivo immunogenicity is a second approach for functional testing of polynucleotides, e.g. minigenes. Transgenic mice expressing appropriate human HLA proteins are immunized with the polynucleotide, e.g. DNA, product. The dose and route of administration are formulation dependent (e.g., IM for polynucleotide (e.g., naked DNA or PVP-formulated DNA) in PBS, intraperitoneal (IP) for lipid-complexed polynucleotide (e.g., DNA)). Eleven to twenty-one days after immunization, splenocytes are harvested and restimulated for one week in the presence of polynucleotides encoding each peptide being tested. Thereafter, for peptides comprising or consisting of variants, standard assays are conducted to determine if there is cytolysis of peptide-loaded, ⁵¹Cr-labeled target cells. Once again, lysis of target cells that were exposed to variants corresponding to those encoded by the polynucleotide (e.g. minigene) demonstrates polynucleotide (e.g., DNA) vaccine function and induction of CTLs. Immunogenicity of HTL epitopes is evaluated in transgenic mice in an analogous manner.

[00238] Alternatively, the nucleic acids can be administered using ballistic delivery as described, for instance, in U.S. Patent No. 5,204,253. Using this technique, particles comprised solely of a polynucleotide such as DNA are administered. In a further alternative embodiment for ballistic delivery, polynucleotides such as DNA can be adhered to particles, such as gold particles.

The use of polynucleotides such as multi-epitope minigenes is described herein and in, e.g. co-pending application U.S.S.N. 09/311,784; Ishioka et al., J. Immunol. 162:3915-3925, 1999; An, L. and Whitton, J. L., J. Virol. 71:2292, 1997; Thomson, S. A. et al., J. Immunol. 157:822, 1996; Whitton, J. L. et al., J. Virol. 67:348, 1993; Hanke, R. et al., Vaccine 16:426, 1998. For example, a polynucleotide such as a multi-epitope DNA plasmid can be engineered which encodes an epitope derived from multiple regions of a infectious agent (e.g., p53, HER2/nev, MAGE-2/3, or CEA), a pan-DR binding peptide such as the PADRE® universal helper T cell epitope, and an endoplasmic reticulum-translocating signal sequence. As descibed in the sections above, a peptide/polynucleotide may also comprise/encode epitopes that are derived from other infectious agents.

[00240] Thus, the invention includes peptides as described herein, polynucleotides encoding each of said peptides, as well as compositions comprising the peptides and polynucleotides, and includes methods for producing and methods of using the peptides, polynucleotides, and compositions, as further described below.

- [00241] Compositions. In other embodiments, the invention is directed to a composition comprising one or more peptides and/or polynucleotides of the invention and optionally another component(s).
- [00242] In some embodiments, the composition comprises or consists of multiple peptides, e.g., 2, 3, 4, 5, 6, 7, 8, or 9 peptides of the invention. In some embodiments, the composition comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 peptides of the invention. Combinations of peptides include, for example, a peptide comprising or alternatively consisting of the Gag 545 variant EPLTSLKSLF (SEQ ID NO:[[_]] 1) and a peptide comprising or alternatively consisting of the Gag 545 variant YPLASLKSLF (SEQ ID NO:[[_]] 2), or combinations of peptides from different tables in Tables 6-9 and/or Figures 1A-4.
- [00243] Compositions of the invention may comprise polynucleotides encoding the above peptides and/or combinations of peptides.
- [00244] The composition can comprise at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 peptides and/or polynucleotides selected from those described above or below. At least one of the one or more peptides can be a heteropolymer or a homopolymer. Additionally, the composition can comprise a CTL and/or HTL epitope, which can be derived from a tumor-associated antigen. The additional epitope can also be a PanDR binding molecule, (e.g., a PADRE® universal helper T cell epitope).
- [00245] Optional components include excipients, diluents, proteins such as peptides comprising a CTL epitope, and/or an HTL epitope such as a pan-DR binding peptide (e.g., a PADRE® universal helper T cell epitope), and/or a carrier, polynucleotides encoding such proteins, lipids, or liposomes, as well as other components described herein. There are numerous embodiments of compositions in accordance with the invention, such as a cocktail of one or more peptides and/or polynucleotides (e.g., minigenes); a cocktail of one or more peptides and/or polynucleotides (e.g., minigenes) and one or more CTL and/or HTL epitopes.
- [00246] Compositions may comprise one or more peptides (and/or polynucleotides such as minigenes) of the invention, along with one or more other components as described above and herein. "One or more" refers to any whole unit integer from 1-150, e.g., at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100,

105, 110, 115, 120, 125, 130, 135, 140, 145, or 150 peptides, polynucleotides, or other components.

Compositions of the invention may be, for example, polynucleotides or [00247] polypeptides of the invention combined with or complexed to cationic lipid formulations; lipopeptides (e.g., Vitiello, A. et al., J. Clin. Invest. 95:341, 1995), encapsulated e.g., in poly(DL-lactide-co-glycolide) ("PLG") microspheres (see, e.g., Eldridge, et al., Molec. Immunol. 28:287-294, 1991: Alonso et al., Vaccine 12:299-306, 1994; Jones et al., Vaccine 13:675-681, 1995); peptide compositions contained in immune stimulating complexes (ISCOMS) (see, e.g., Takahashi et al., Nature 344:873-875, 1990; Hu et al., Clin Exp Immunol. 113:235-243, 1998); multiple antigen peptide systems (MAPs) (see e.g., Tam, J. P., Proc. Natl. Acad. Sci. U.S.A. 85:5409-5413, 1988; Tam, J.P., J. Immunol. Methods 196:17-32, 1996); viral, bacterial, or, fungal delivery vectors (Perkus, M. E. et al., In: Concepts in vaccine development, Kaufmann, S. H. E., ed., p. 379, 1996; Chakrabarti, S. et al., Nature 320:535, 1986; Hu, S. L. et al., Nature 320:537, 1986; Kieny, M.-P. et al., AIDS Bio/Technology 4:790, 1986; Top, F. H. et al., J. Infect. Dis. 124:148, 1971; Chanda, P. K. et al., Virology 175:535, 1990); particles of viral or synthetic origin (e.g., Kofler, N. et al., J. Immunol. Methods. 192:25, 1996; Eldridge, J. H. et al., Sem. Hematol. 30:16, 1993; Falo, L. D., Jr. et al., Nature Med. 7:649, 1995); adjuvants (e.g., incomplete Freund's adjuvant) (Warren, H. S., Vogel, F. R., and Chedid, L. A. Annu. Rev. Immunol. 4:369, 1986; Gupta, R. K. et al., Vaccine 11:293, 1993); liposomes (Reddy, R. et al., J. Immunol. 148:1585, 1992; Rock, K. L., Immunol. Today 17:131, 1996); or, particle-absorbed cDNA or other polynucleotides of the invention (Ulmer, J. B. et al., Science 259:1745, 1993; Robinson, H. L., Hunt, L. A., and Webster, R. G., Vaccine 11:957, 1993; Shiver, J. W. et al., In: Concepts in vaccine development, Kaufmann, S. H. E., ed., p. 423, 1996; Cease, K. B., and Berzofsky, J. A., Annu. Rev. Immunol. 12:923, 1994 and Eldridge, J. H. et al., Sem. Hematol. 30:16, 1993), etc. Toxintargeted delivery technologies, also known as receptor mediated targeting, such as those of Avant Immunotherapeutics, Inc. (Needham, Massachusetts) or attached to a stress protein, e.g., HSP 96 (Stressgen Biotechnologies Corp., Victoria, BC, Canada) can also be used.

[00248] Compositions of the invention comprise polynucleotide-mediated modalities. DNA or RNA encoding one or more of the peptides of the invention can be administered to a patient. This approach is described, for instance, in Wolff et. al., Science 247:1465 (1990) as well as U.S. Patent Nos. 5,580,859; 5,589,466; 5,804,566; 5,739,118; 5,736,524;

5,679,647; and, WO 98/04720. Examples of DNA-based delivery technologies include "naked DNA", facilitated (bupivicaine, polymers (e.g., PVP, PINC, etc.), peptidemediated) delivery, cationic lipid complexes, and particle-mediated ("gene gun") or pressure-mediated delivery (see, e.g., U.S. Patent No. 5,922,687). Accordingly, peptides of the invention can be expressed by viral or bacterial vectors. Examples of expression vectors include attenuated viral hosts, such as Modified Vaccinia Ankara (MVA) (e.g., Bavarian Noridic), vaccinia or fowlpox. For example, vaccinia virus is used as a vector to express nucleotide sequences that encode the peptides of the invention. Upon introduction into an acutely or chronically infected host or into a non-infected host, the recombinant vaccinia virus expresses the immunogenic peptide, and thereby elicits an immune response. Vaccinia vectors and methods useful in immunization protocols are described in, e.g., U.S. Patent No. 4,722,848. Another vector is BCG (Bacille Calmette Guerin). BCG vectors are described in Stover et al., Nature 351:456-460 (1991). A wide variety of other vectors useful for the apeutic administration or immunization of the peptides of the invention, e.g. adeno and adeno-associated virus vectors, alpha virus vectors, retroviral vectors, Salmonella typhi vectors, detoxified anthrax toxin vectors, and the like, are apparent to those skilled in the art from the description herein.

- [00249] In certain embodiments, components that induce T cell responses are combined with components that induce antibody responses to the target antigen of interest. A preferred embodiment of such a composition comprises class I and class II epitopes in accordance with the invention. Alternatively, a composition comprises a class I and/or class II epitope in accordance with the invention, along with a PADRE® molecule (Epimmune, San Diego, CA).
- [00250] Compositions of the invention can comprise antigen presenting cells, such as dendritic cells. Antigen presenting cells, e.g., dendritic cells, may be transfected, e.g., with a polynucleotide such as a minigene construct in accordance with the invention, in order to elicit immune responses. The peptide can be bound to an HLA molecule on the antigenresenting cell, whereby when an HLA-restricted cytotoxic T lymphocyte (CTL) is present, a receptor of the CTL binds to a complex of the HLA molecule and the peptide.
- [00251] The compositions of the invention may also comprise antiviral drugs such as interferon-α, or immune adjuvants such as IL-12, GM-CSF, etc.
- [00252] Compositions may comprise an HLA heavy chain, β_2 -microglobulin, streptavidin, and/or biotin. The streptavidin may be fluorescently labeled. Compositions may comprise

tetramers (see e.g., U.S. Pat. No. 5,635,363; Science 274:94-96 (1996)). A tetramer composition comprising an HLA heavy chain, β₂-microglobulin, streptavidin, and biotin. The streptavidin may be fluorescently labeled. Compositions may also comprise dimers. A dimer composition comprises as MHC molecule and an Ig molecule (see e.g., PNAS 95:7568-73 (1998)).

In some embodiments it may be desirable to include in the compositions of the invention at least one component which primes cytotoxic T lymphocytes. Lipids have been identified as agents capable of priming CTL in vivo against viral antigens. For example, palmitic acid residues can be attached to the ε-and α- amino groups of a lysine residue and then linked, e.g., via one or more linking residues such as Gly, Gly-Gly-, Ser, Ser-Ser, or the like, to an immunogenic peptide. The lipidated peptide can then be administered either directly in a micelle or particle, incorporated into a liposome, or emulsified in an adjuvant, e.g., incomplete Freund's adjuvant. A preferred composition comprises palmitic acid attached to ε- and α- amino groups of Lys, which is attached via linkage, e.g., Ser-Ser, to the amino terminus of the peptide.

[00254] As another example of lipid priming of CTL responses, *E. coli* lipoproteins, such as tripalmitoyl-S-glycerylcysteinlyseryl-serine (P₃CSS) can be used to prime virus specific CTL when covalently attached to an appropriate peptide (see, e.g., Deres, et al., Nature 342:561, 1989). Peptides of the invention can be coupled to P₃CSS, for example, and the lipopeptide administered to an individual to specifically prime a CTL response to the target antigen. Moreover, because the induction of neutralizing antibodies can also be primed with P₃CSS-conjugated epitopes, two such compositions can be combined to more effectively elicit both humoral and cell-mediated responses.

[00255] Another preferred embodiment is a composition comprising one or more peptides of the invention emulsified in IFA.

[00256] Compositions of the invention may also comprise CTL and/or HTL peptides. Such CTL and HTL peptides can be modified by the addition of amino acids to the termini of a peptide to provide for ease of linking peptides one to another, for coupling to a carrier support or larger peptide, for modifying the physical or chemical properties of the peptide or oligopeptide, or the like. Amino acids such as tyrosine, cysteine, lysine, glutamic or aspartic acid, or naturally or unnaturally occuring amino acid residues, can be introduced at the carboxyl- or amino-terminus of the peptide or oligopeptide, particularly class I peptides. However, it is to be noted that modification at the carboxyl terminus of a CTL

epitope may, in some cases, alter binding characteristics of the peptide. In addition, the peptide or oligopeptide sequences can differ from the natural sequence by being modified by terminal-NH₂ acylation, *e.g.*, by alkanoyl (C₁-C₂₀) or thioglycolyl acetylation, terminal-carboxyl amidation, *e.g.*, ammonia, methylamine, *etc.* In some instances these modifications may provide sites for linking to a support or other molecule. CTL and HTL epitopes may comprise additional amino acids, such as those described above including spacers.

- [00257] A further embodiment of a composition in accordance with the invention is an antigen presenting cell that comprises one or more peptides in accordance with the invention. The antigen presenting cell can be a "professional" antigen presenting cell, such as a dendritic cell. The antigen presenting cell can comprise the peptide of the invention by any means known or to be determined in the art. Such means include pulsing of dendritic cells with one or more individual peptides, by nucleic acid administration such as ballistic nucleic acid delivery or by other techniques in the art for administration of nucleic acids, including vector-based, e.g. viral vector, delivery of nucleic acids.
- [00258] Compositions may comprise carriers. Carriers that can be used with compositions of the invention are well known in the art, and include, e.g., thyroglobulin, albumins such as human serum albumin, tetanus toxoid, polyamino acids such as poly L-lysine, poly L-glutamic acid, influenza virus proteins, hepatitis B virus core protein, and the like.
- [00259] The compositions (e.g. pharmaceutical compositions) can contain a physiologically tolerable diluent such as water, or a saline solution, preferably phosphate buffered saline. Additionally, as disclosed herein, CTL responses can be primed by conjugating peptides of the invention to lipids, such as tripalmitoyl-S-glyceryl-cysteinyl-seryl-serine (P₃CSS).
- [00260] Compositions of the invention may be pharmaceutically acceptable compositions. Pharmaceutical compositions preferably contain an immunologically effective amount of one or more peptides and/or polynucleotides of the invention, and optionally one or more other components which are pharmaceutically acceptable. A preferred composition comprises one or more peptides of the invention and IFA. A more preferred composition of the invention comprises one or more peptides of the invention, one or more peptides, and IFA.
- [00261] Upon immunization with a peptide and/or polynucleotide and/or composition in accordance with the invention, via injection (e.g., SC, ID, IM), aerosol, oral, transdermal, transmucosal, intrapleural, intrathecal, or other suitable routes, the immune system of the

host responds to the vaccine by an immune response comprising the production of antibodies, CTLs and/or HTLs specific for the desired antigen(s). Consequently, the host becomes at least partially immune to subsequent exposure to the infectious agent(s), or at least partially resistant to further development of infectious agent-bearing cells and thereby derives a prophylactic or therapeutic benefit.

[00262] Furthermore, the peptides, primers, and epitopes of the invention can be used in any desired immunization or administration regimen; e.g., as part of periodic vaccinations such as annual vaccinations as in the veterinary arts or as in periodic vaccinations as in the human medical arts, or as in a prime-boost regime wherein an inventive vector or recombinant is administered either before or after the administration of the same or of a different epitope of interest or recombinant or vector expressing such as a same or different epitope of interest (including an inventive recombinant or vector expressing such as a same or different epitope of interest), see, e.g., U.S. Pat. Nos. 5,997,878; 6,130,066; 6,180,398; 6,267,965; and 6,348,450. An useful viral vector of the present invention is Modified Vaccinia Ankara (MVA) (e.g., Bavarian Noridic (MVA-BN)).

Recent studies have indicated that a prime-boost protocol, whereby immunization [00263] with a poxvirus recombinant expressing a foreign gene product is followed by a boost using a purified subunit preparation form of that gene product, elicits an enhanced immune response relative to the response elicited with either product alone. Human volunteers immunized with a vaccinia recombinant expressing the HIV-1 envelope glycoprotein and boosted with purified HIV-1 envelope glycoprotein subunit preparation exhibit higher HIV-1 neutralizing antibody titers than individuals immunized with just the vaccinia recombinant or purified envelope glycoprotein alone (Graham et al., J. Infect. Dis., 167:533-537 (1993); Cooney et al., Proc. Natl. Acad. Sci. USA, 90:1882-1886 (1993)). Humans immunized with two injections of an ALVAC-HIV-1 env recombinant (vCP125) failed to develop HIV specific antibodies. Boosting with purified rgp160 from a vaccinia virus recombinant resulted in detectable HIV-1 neutralizing antibodies. Furthermore, specific lymphocyte T cell proliferation to rgp160 was clearly increased by the boost with rgp160. Envelope specific cytotoxic lymphocyte activity was also detected with this vaccination regimen (Pialoux et al., AIDS Res. and Hum. Retroviruses, 11:272-381 (1995)). Macaques immunized with a vaccinia recombinant expressing the simian immunodeficiency virus (SIV) envelope glycoprotein and boosted with SIV envelope glycoprotein from a baculovirus recombinant are protected against SIV challenge (Hu et al., AID Res. and Hum. Retroviruses, 3:615-620 (1991); Hu et al., Science 255:456-459 (1992)). In the same fashion, purified HCMVgB protein can be used in prime-boost protocols with NYVAC or ALVAC-gB recombinants.

[00264] In certain embodiments, the polynucleotides are complexed in a liposome preparation. Liposomal preparations for use in the instant invention include cationic (positively charged), anionic (negatively charged) and neutral preparations. However, cationic liposomes are particularly preferred because a tight charge complex can be formed between the cationic liposome and the polyanionic nucleic acid. Cationic liposomes have been shown to mediate intracellular delivery of plasmid DNA (Felgner et al., Proc. Natl. Acad. Sci. USA 84:74137416 (1987), which is herein incorporated by reference); mRNA (Malone et al., Proc. Natl. Acad. Sci. USA 86:60776081 (1989), which is herein incorporated by reference); and purified transcription factors (Debs et al., J. Biol. Chem. 265:1018910192 (1990), which is herein incorporated by reference), in functional form.

[00265] Cationic liposomes are readily available. For example, N-[12,3-dioleyloxy)-propyl]-N,N,N-triethylammonium (DOTMA) liposomes are particularly useful and are available under the trademark Lipofectin, from GIBCO BRL, Grand Island, N.Y. (See, also, Felgner *et al.*, *Proc. Natl Acad. Sci. USA 84*:74137416 (1987)). Other commercially available liposomes include transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer).

[00266] Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g. PCT Publication No. WO 90/11092 for a description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-(trimethylammonio)propane) liposomes. Preparation of DOTMA liposomes is explained in the literature, see, e.g., P. Felgner et al., Proc. Natl. Acad. Sci. USA 84:74137417. Similar methods can be used to prepare liposomes from other cationic lipid materials.

[00267] Similarly, anionic and neutral liposomes are readily available, such as from Avanti Polar Lipids (Birmingham, Ala.), or can be easily prepared using readily available materials. Such materials include phosphatidyl, choline, cholesterol, phosphatidyl ethanolamine, dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), dioleoylphoshatidyl ethanolamine (DOPE), among others. These materials can also be mixed with the DOTMA and DOTAP starting materials in appropriate ratios. Methods for making liposomes using these materials are well known in the art.

[00268] For example, commercially available dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), and dioleoylphosphatidyl ethanolamine (DOPE) can be used in various combinations to make conventional liposomes, with or without the addition of cholesterol. Thus, for example, DOPG/DOPC vesicles can be prepared by drying 50 mg each of DOPG and DOPC under a stream of nitrogen gas into a sonication vial. The sample is placed under a vacuum pump overnight and is hydrated the following day with deionized water. The sample is then sonicated for 2 hours in a capped vial, using a Heat Systems model 350 sonicator equipped with an inverted cup (bath type) probe at the maximum setting while the bath is circulated at 15EC. Alternatively, negatively charged vesicles can be prepared without sonication to produce multilamellar vesicles or by extrusion through nucleopore membranes to produce unilamellar vesicles of discrete size. Other methods are known and available to those of skill in the art.

[00269] The liposomes can comprise multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), or large unilamellar vesicles (LUVs), with SUVs being preferred. The various liposome nucleic acid complexes are prepared using methods well known in the See, e.g., Straubinger et al., Methods of Immunology 101:512527 (1983). For example, MLVs containing nucleic acid can be prepared by depositing a thin film of phospholipid on the walls of a glass tube and subsequently hydrating with a solution of the material to be encapsulated. SUVs are prepared by extended sonication of MLVs to produce a homogeneous population of unilamellar liposomes. The material to be entrapped is added to a suspension of preformed MLVs and then sonicated. When using liposomes containing cationic lipids, the dried lipid film is resuspended in an appropriate solution such as sterile water or an isotonic buffer solution such as 10 mM Tris/NaCl, sonicated, and then the preformed liposomes are mixed directly with the DNA. The liposome and DNA form a very stable complex due to binding of the positively charged liposomes to the cationic DNA. SUVs find use with small nucleic acid fragments. LUVs are prepared by a number of methods, well known in the art. Commonly used methods include Ca²⁺-EDTA chelation (Papahadjopoulos et al., Biochim. Biophys. Acta 394:483 (1975); Wilson et al., Cell 17:77 (1979)); ether injection (Deamer, D. and Bangham, A., Biochim. Biophys. Acta 443:629 (1976); Ostro et al., Biochem. Biophys. Res. Commun. 76:836 (1977); Fraley et al., Proc. Natl. Acad. Sci. USA 76:3348 (1979)); detergent dialysis (Enoch, H. and Strittmatter, P., Proc. Natl. Acad. Sci. USA 76:145 (1979)); and reversephase evaporation (REV) (Fraley et al., J. Biol. Chem. 255:10431 (1980); Szoka, F.

and Papahadjopoulos, D., Proc. Natl. Acad. Sci. USA 75:145 (1978); SchaeferRidder et al., Science 215:166 (1982)).

- [00270] Generally, the ratio of DNA to liposomes will be from about 10:1 to about 1:10. Preferably, the ration will be from about 5:1 to about 1:5. More preferably, the ration will be about 3:1 to about 1:3. Still more preferably, the ratio will be about 1:1.
- [00271] U.S. Patent No. 5,676,954 reports on the injection of genetic material, complexed with cationic liposome carriers, into mice. U.S. Patent Nos. 4,897,355, 4,946,787, 5,049,386, 5,459,127, 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 provide cationic lipids for use in transfecting DNA into cells and mammals. U.S. Patent Nos. 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 provide methods for delivering DNA-cationic lipid complexes to mammals.

Binding Affinity of Variants for HLA Molecules

- [00272] As indicated herein, the large degree of HLA polymorphism is an important factor to be taken into account with the epitope-based approach to developing therapeutics and diagnostics. To address this factor, epitope selection encompassing identification of peptides capable of binding at high or intermediate affinity to multiple HLA molecules is preferably utilized, most preferably these epitopes bind at high or intermediate affinity to two or more allele-specific HLA molecules. However, in some embodiments, it is preferred that all epitopes in a given composition bind to the alleles of a single HLA supertype or a single HLA molecule.
- [00273] Variants of the invention preferably include those that have an IC₅₀ or binding affinity value for a class I HLA molecule(s) of 500 nM or better (i.e., the value is \leq 500 nM). In certain embodiments of the invention, peptides of interest have an IC₅₀ or binding affinity value for a class I HLA molecule(s) of 200 nM or better. In certain embodiments of the invention, peptides of interest, such as A1 and A24 peptides, have an IC₅₀ or binding affinity value for a class I HLA molecule(s) of 100 nM or better. If HTL epitopes are included, they preferably are HTL epitopes that have an IC₅₀ or binding affinity value for class II HLA molecules of 1000 nM or better, (i.e., the value is \leq 1,000 nM). For example, peptide binding is assessed by testing the capacity of a candidate peptide to bind to a purified HLA molecule in vitro. Peptides exhibiting high or intermediate affinity are

then considered for further analysis. Selected peptides are generally tested on other members of the supertype family. In preferred embodiments, peptides that exhibit cross-reactive binding are then used in cellular screening analyses or vaccines.

[00274] The relationship between binding affinity for HLA class I molecules and immunogenicity of discrete peptide epitopes on bound antigens was determined for the first time by inventors at Epimmune. As disclosed in greater detail herein, higher HLA binding affinity is correlated with greater immunogenicity.

Greater immunogenicity can be manifested in several different ways. [00275] Immunogenicity corresponds to whether an immune response is elicited at all, and to the vigor of any particular response, as well as to the extent of a population in which a response is elicited. For example, a peptide might elicit an immune response in a diverse array of the population, yet in no instance produce a vigorous response. In accordance with these principles, close to 90% of high binding peptides have been found to elicit a response and thus be "immunogenic," as contrasted with about 50% of the peptides that bind with intermediate affinity. (See, e.g., Schaeffer et al. PNAS (1988)) High affinitybinding class I peptides generally have an affinity of less than or equal to 100 nM. Moreover, not only did peptides with higher binding affinity have an enhanced probability of generating an immune response, the generated response tended to be more vigorous than the response seen with weaker binding peptides. As a result, less peptide is required to elicit a similar biological effect if a high affinity binding peptide is used rather than a lower affinity one. Thus, in some preferred embodiments of the invention, high affinity binding epitopes are used.

The correlation between binding affinity and immunogenicity was analyzed by the present inventors by two different experimental approaches (see, e.g., Sette, et al., J. Immunol. 153:5586-5592 (1994)). In the first approach, the immunogenicity of potential epitopes ranging in HLA binding affinity over a 10,000-fold range was analyzed in HLA-A*0201 transgenic mice. In the second approach, the antigenicity of approximately 100 different hepatitis B virus (HBV)-derived potential epitopes, all carrying A*0201 binding motifs, was assessed by using PBL from acute hepatitis patients. Pursuant to these approaches, it was determined that an affinity threshold value of approximately 500 nM (preferably 50 nM or less) determines the capacity of a peptide epitope to elicit a CTL response. These data are true for class I binding affinity measurements for naturally processed peptides and for synthesized T cell epitopes. These data also indicate the

important role of determinant selection in the shaping of T cell responses (see, e.g., Schaeffer et al. Proc. Natl. Acad. Sci. USA 86:4649-4653 (1989)).

- [00277] An affinity threshold associated with immunogenicity in the context of HLA class II (i.e., HLA DR) molecules has also been delineated (see, e.g., Southwood et al. J. Immunology 160:3363-3373 (1998), and U.S. Patent No. 6,413,527, issued July 2, 2002). In order to define a biologically significant threshold of HLA class II binding affinity, a database of the binding affinities of 32 DR-restricted epitopes for their restricting element (i.e., the HLA molecule that binds the epitope) was compiled. In approximately half of the cases (15 of 32 epitopes), DR restriction was associated with high binding affinities, i.e. binding affinity values of 100 nM or less. In the other half of the cases (16 of 32), DR restriction was associated with intermediate affinity (binding affinity values in the 100-1000 nM range). In only one of 32 cases was DR restriction associated with an IC50 of 1000 nM or greater. Thus, 1000 nM is defined as an affinity threshold associated with immunogenicity in the context of DR molecules.
- [00278] The binding affinity of peptides for HLA molecules can be determined as described in Example 1, below.

Enhancing Population Coverage of the Vaccine

- [00279] The primary anchor residues of the HLA class I peptide epitope supermotifs and motifs are summarized in Tables 1-2. Allele-specific HLA molecules that are comprised by the various HLA class I supertypes are listed in Table 4. In some cases, patterns of amino acid residues are present in both a motif and a supermotif. The relationship of a particular motif and any related supermotif is indicated in the description of the individual motifs.
- [00280] By inclusion of one or more epitopes from several motifs or supermotifs in a vaccine composition, enhanced population coverage for major global ethnicities can be obtained.

Assays to Detect T-Cell Responses

[00281] Once HLA binding peptides are identified, they can be tested for the ability to elicit a T-cell response. The preparation and evaluation of motif-bearing peptides are described, e.g., in PCT publications WO 94/20127 and WO 94/03205. Briefly, peptides

comprising epitopes from a particular antigen are synthesized and tested for their ability to bind to relevant HLA proteins. These assays may involve evaluation of peptide binding to purified HLA class I molecules in relation to the binding of a radioiodinated reference peptide. Alternatively, cells expressing empty class I molecules (*i.e.* cell surface HLA molecules that lack any bound peptide) may be evaluated for peptide binding by immunofluorescent staining and flow microfluorimetry. Other assays that may be used to evaluate peptide binding include peptide-dependent class I assembly assays and/or the inhibition of CTL recognition by peptide competition. Those peptides that bind to an HLA class I molecule, typically with an affinity of 500 nM or less, are further evaluated for their ability to serve as targets for CTLs derived from infected or immunized individuals, as well as for their capacity to induce primary *in vitro* or *in vivo* CTL responses that can give rise to CTL populations capable of reacting with selected target cells associated with pathology.

[00282] Analogous assays are used for evaluation of HLA class II binding peptides. HLA class II motif-bearing peptides that are shown to bind, typically at an affinity of 1000 nM or less, are further evaluated for the ability to stimulate HTL responses.

[00283] Conventional assays utilized to detect T cell responses include proliferation assays, lymphokine secretion assays, direct cytotoxicity assays, and limiting dilution assays. For example, antigen-presenting cells that have been incubated with a peptide can be assayed for the ability to induce CTL responses in responder cell populations. Antigen-presenting cells can be normal cells such as peripheral blood mononuclear cells or dendritic cells. Alternatively, mutant, non-human mammalian cell lines that have been transfected with a human class I MHC gene, and that are deficient in their ability to load class I molecules with internally processed peptides, are used to evaluate the capacity of the peptide to induce in vitro primary CTL responses. Peripheral blood mononuclear cells (PBMCs) can be used as the source of CTL precursors. Antigen presenting cells are incubated with peptide, after which the peptide-loaded antigen-presenting cells are then incubated with the responder cell population under optimized culture conditions. Positive CTL activation can be determined by assaying the culture for the presence of CTLs that lyse radio-labeled target cells, either specific peptide-pulsed targets or target cells that express endogenously processed antigen from which the specific peptide was derived. Alternatively, the presence of epitope-specific CTLs can be determined by IFNy in situ ELISA.

- [00284] In an embodiment of the invention, directed to diagnostics, a method has been devised which allows direct quantification of antigen-specific T cells by staining with fluorescein-labelled HLA tetrameric complexes (Altman, J. D. et al., Proc. Natl. Acad. Sci. USA 90:10330, 1993; Altman, J. D. et al., Science 274:94, 1996). Other options include staining for intracellular lymphokines, and interferon release assays or ELISPOT assays. Tetramer staining, intracellular lymphokine staining and ELISPOT assays all appear to be at least 10-fold more sensitive than more conventional assays (Lalvani, A. et al., J. Exp. Med. 186:859, 1997; Dunbar, P. R. et al., Curr. Biol. 8:413, 1998; Murali-Krishna, K. et al., Immunity 8:177, 1998). Additionally, DimerX technology can be used as a means of quantitation (see, e.g., Science 274:94-99 (1996) and Proc. Natl. Acad. Sci. 95:7568-73 (1998)).
- [00285] HTL activation may also be assessed using techniques known to those in the art, such as T cell proliferation or lymphokine secretion (see, e.g. Alexander et al., Immunity 1:751-761, 1994).
- [00286] Alternatively, immunization of HLA transgenic mice can be used to determine immunogenicity of peptide epitopes. Several transgenic mouse strains, e.g., mice with human A2.1, A11 (which can additionally be used to analyze HLA-A3 epitopes), and B7 alleles have been characterized. Other transgenic mice strains (e.g., transgenic mice for HLA-A1 and A24) are being developed. Moreover, HLA-DR1 and HLA-DR3 mouse models have been developed. In accordance with principles in the art, additional transgenic mouse models with other HLA alleles are generated as necessary.
- [00287] Such mice can be immunized with peptides emulsified in Incomplete Freund's Adjuvant; thereafter any resulting T cells can be tested for their capacity to recognize target cells that have been peptide-pulsed or transfected with genes encoding the peptide of interest. CTL responses can be analyzed using cytotoxicity assays described above. Similarly, HTL responses can be analyzed using, e.g., T cell proliferation or lymphokine secretion assays.

Minigenes

[00288] A number of different approaches are available which allow simultaneous delivery of multiple epitopes. Nucleic acids encoding multiple epitopes are a useful embodiment of the invention; discrete peptide epitopes or polyepitopic peptides can be encoded. The

epitopes to be included in a minigene are preferably selected according to the guidelines set forth in the previous section. Examples of amino acid sequences that can be included in a minigene include: HLA class I epitopes, HLA class II epitopes, a ubiquitination signal sequence, and/or a targeting sequence such as an endoplasmic reticulum (ER) signal sequence to facilitate movement of the resulting peptide into the endoplasmic reticulum. Examples of minigene constructs are shown in Tables 23-28.

[00289] The use of multi-epitope minigenes is also described in, e.g., co-pending applications U.S.S.N. 09/311,784, 09/894,018, 60/419,973, 60/415,463; Ishioka et al., J. Immunol. 162:3915-3925, 1999; An, L. and Whitton, J. L., J. Virol. 71:2292, 1997; Thomson, S. A. et al., J. Immunol. 157:822, 1996; Whitton, J. L. et al., J. Virol. 67:348, 1993; Hanke, R. et al., Vaccine 16:426, 1998. For example, a multi-epitope DNA plasmid encoding nine dominant HLA-A*0201- and A11-restricted CTL epitopes derived from the polymerase, envelope, and core proteins of HBV and human immunodeficiency virus (HIV), a PADRE® universal helper T cell (HTL) epitope, and an endoplasmic reticulumtranslocating signal sequence has been engineered. Immunization of HLA transgenic mice with this plasmid construct resulted in strong CTL induction responses against the nine CTL epitopes tested. This CTL response was similar to that observed with a lipopeptide of known immunogenicity in humans, and significantly greater than immunization using peptides in oil-based adjuvants. Moreover, the immunogenicity of DNA-encoded epitopes in vitro was also correlated with the in vitro responses of specific CTL lines against target cells transfected with the DNA plasmid. These data show that the minigene served: 1.) to generate a CTL response and 2.) to generate CTLs that recognized cells expressing the encoded epitopes. A similar approach can be used to develop minigenes encoding epitopes of an infectious agent.

[00290] For example, to create a DNA sequence encoding the selected epitopes (minigene) for expression in human cells, the amino acid sequences of the epitopes may be reverse translated. A human codon usage table can be used to guide the codon choice for each amino acid. These epitope-encoding DNA sequences may be directly adjoined, so that when translated, a continuous peptide sequence is created. However, to optimize expression and/or immunogenicity, additional elements can be incorporated into the minigene design such as spacer amino acid residues between epitopes. HLA presentation of CTL and HTL epitopes may be improved by including synthetic (e.g. poly-alanine) or naturally-occurring flanking sequences adjacent to the CTL or HTL epitopes; these larger

peptides comprising the epitope(s) are within the scope of the invention. In one embodiment, spacer amino acid residues between one or more CTL and/or HTL epitopes are designed so as to minimize junctional epitopes that may result from the juxtaposition of 2 CTL and/or HTL epitopes.

- [00291] The minigene sequence may be converted to DNA by assembling oligonucleotides that encode the plus and minus strands of the minigene. Overlapping oligonucleotides (30-100 bases long) may be synthesized, phosphorylated, purified and annealed under appropriate conditions using well known techniques. The ends of the oligonucleotides can be joined, for example, using T4 DNA ligase. This synthetic minigene, encoding the epitope peptide, can then be cloned into a desired expression vector.
- [00292] Standard regulatory sequences well known to those of skill in the art are preferably included in the vector to ensure expression in the target cells. Several vector elements are desirable: a promoter with a downstream cloning site for minigene insertion; a polyadenylation signal for efficient transcription termination; an *E. coli* origin of replication; and an *E. coli* selectable marker (e.g. ampicillin or kanamycin resistance). Numerous promoters can be used for this purpose, e.g., the human cytomegalovirus (hCMV) CMV-IE promoter. See, e.g., U.S. Patent Nos. 5,580,859 and 5,589,466 for other suitable promoter sequences.
- [00293] Optimized peptide expression and immunogenicity can be achieved by certain modifications to a minigene construct. For example, in some cases introns facilitate efficient gene expression, thus one or more synthetic or naturally-occurring introns can be incorporated into the transcribed region of the minigene. The inclusion of mRNA stabilization sequences and sequences for replication in mammalian cells may also be considered for increasing minigene expression.
- [00294] Once an expression vector is selected, the minigene is cloned into the polylinker region downstream of the promoter. This plasmid is transformed into an appropriate bacterial strain, and DNA is prepared using standard techniques. The orientation and DNA sequence of the minigene, as well as all other elements included in the vector, are confirmed using restriction mapping, PCR and/or DNA sequence analysis. Bacterial cells harboring the correct plasmid can be stored as cell banks.
- [00295] In addition, immunostimulatory sequences (ISSs or CpGs) appear to play a role in the immunogenicity of DNA vaccines. These sequences may be included in the vector, outside the minigene coding sequence to enhance immunogenicity.

[00296] In some embodiments, a bi-cistronic expression vector which allows production of both the minigene-encoded epitopes and a second protein (e.g., one that modulates immunogenicity) can be used. Examples of proteins or polypeptides that, if co-expressed with epitopes, can enhance an immune response include cytokines (e.g., IL-2, IL-12, GM-CSF), cytokine-inducing molecules (e.g., LeIF), costimulatory molecules, or pan-DR binding proteins (PADRE®, Epimmune, San Diego, CA). Helper T cell (HTL) epitopes such as PADRE® molecules can be joined to intracellular targeting signals and expressed separately from expressed CTL epitopes. This can be done in order to direct HTL epitopes to a cell compartment different than that of the CTL epitopes, one that provides for more efficient entry of HTL epitopes into the HLA class II pathway, thereby improving HTL induction. In contrast to HTL or CTL induction, specifically decreasing the immune response by co-expression of immunosuppressive molecules (e.g. TGF-β) may be beneficial in certain diseases.

[00297] Therapeutic quantities of plasmid DNA can be produced for example, by fermentation in *E. coli*, followed by purification. Aliquots from the working cell bank are used to inoculate growth medium, and are grown to saturation in shaker flasks or a bioreactor according to well known techniques. Plasmid DNA is purified using standard bioseparation technologies such as solid phase anion-exchange resins available, *e.g.*, from QIAGEN, Inc. (Valencia, California). If required, supercoiled DNA can be isolated from the open circular and linear forms using gel electrophoresis or other methods.

[00298] Purified plasmid DNA can be prepared for injection using a variety of formulations. The simplest of these is reconstitution of lyophilized DNA in sterile phosphate-buffer saline (PBS). This approach, known as "naked DNA," is currently being used for intramuscular (IM) administration in clinical trials. To maximize the immunotherapeutic effects of minigene vaccines, alternative methods of formulating purified plasmid DNA may be used. A variety of such methods have been described, and new techniques may become available. Cationic lipids, glycolipids, and fusogenic liposomes can also be used in the formulation (see, e.g., WO 93/24640; Mannino & Gould-Fogerite, BioTechniques 6(7): 682 (1988); U.S. Patent No. 5,279,833; WO 91/06309; and Felgner, et al., Proc. Nat'l Acad. Sci. USA 84:7413 (1987). In addition, peptides and compounds referred to collectively as protective, interactive, non-condensing compounds (PINC) can also be complexed to purified plasmid DNA to influence variables such as stability, intramuscular dispersion, or trafficking to specific organs or cell types.

[00299] Known methods in the art can be used to enhance delivery and uptake of a polynucleotide *in vivo*. For example, the polynucleotide can be complexed to polyvinylpyrrolidone (PVP), to prolong the localized bioavailability of the polynucleotide, thereby enhancing uptake of the polynucleotide by the organisum (see e.g., U.S. Patent No. 6,040,295; EP 0 465 529; WO 98/17814). PVP is a polyamide that is known to form complexes with a wide variety of substances, and is chemically and physiologically inert.

[00300] Target cell sensitization can be used as a functional assay of the expression and HLA class I presentation of minigene-encoded epitopes. For example, the plasmid DNA is introduced into a mammalian cell line that is a suitable target for standard CTL chromium release assays. The transfection method used will be dependent on the final formulation, electroporation can be used for "naked" DNA, whereas cationic lipids or DNA:PVP compositions allow direct *in vitro* transfection. A plasmid expressing green fluorescent protein (GFP) can be co-transfected to allow enrichment of transfected cells using fluorescence activated cell sorting (FACS). The transfected cells are then chromium-51 (51Cr) labeled and used as targets for epitope-specific CTLs. Cytolysis of the target cells, detected by 51Cr release, indicates both the production and HLA presentation of, minigene-encoded CTL epitopes. Expression of HTL epitopes may be evaluated in an analogous manner using assays to assess HTL activity.

[00301] In vivo immunogenicity is a second approach for functional testing of minigene DNA formulations. Transgenic mice expressing appropriate human HLA proteins are immunized with the DNA product. The dose and route of administration are formulation dependent (e.g., IM for DNA in PBS, intraperitoneal (IP) for lipid-complexed DNA). Eleven to twenty-one days after immunization, splenocytes are harvested and restimulated for one week in the presence of peptides encoding each epitope being tested. Thereafter, for CTLs, standard assays are conducted to determine if there is cytolysis of peptide-loaded, ⁵¹Cr-labeled target cells. Once again, lysis of target cells that were exposed to epitopes corresponding to those in the minigene, demonstrates DNA vaccine function and induction of CTLs. Immunogenicity of HTL epitopes is evaluated in transgenic mice in an analogous manner.

[00302] Alternatively, the nucleic acids can be administered using ballistic delivery as described, for instance, in U.S. Patent No. 5,204,253. Using this technique, particles comprised solely of DNA are administered. In a further alternative embodiment for ballistic delivery, DNA can be adhered to particles, such as gold particles.

Vaccine Compositions

[00303] Vaccines that contain an immunologically effective amount of one or more peptides or polynucleotides of the invention are a further embodiment of the invention. The peptides can be delivered by various means or formulations, all collectively referred Such vaccine compositions, and/or modes of to as "vaccine" compositions. administration, can include, for example, naked DNA, DNA formulated with PVP, DNA in cationic lipid formulations; lipopeptides (e.g., Vitiello, A. et al., J. Clin. Invest. 95:341, 1995), DNA or peptides, encapsulated e.g., in poly(DL-lactide-co-glycolide) ("PLG") microspheres (see, e.g., Eldridge, et al., Molec. Immunol. 28:287-294, 1991: Alonso et al., Vaccine 12:299-306, 1994; Jones et al., Vaccine 13:675-681, 1995); peptide compositions contained in immune stimulating complexes (ISCOMS) (see, e.g., Takahashi et al., Nature 344:873-875, 1990; Hu et al., Clin Exp Immunol. 113:235-243, 1998); multiple antigen peptide systems (MAPs) (see e.g., Tam, J. P., Proc. Natl. Acad. Sci. U.S.A. 85:5409-5413, 1988; Tam, J.P., J. Immunol. Methods 196:17-32, 1996); viral, bacterial, or, fungal delivery vectors (Perkus, M. E. et al., In: Concepts in vaccine development, Kaufmann, S. H. E., ed., p. 379, 1996; Chakrabarti, S. et al., Nature 320:535, 1986; Hu, S. L. et al., Nature 320:537, 1986; Kieny, M.-P. et al., AIDS Bio/Technology 4:790, 1986; Top, F. H. et al., J. Infect. Dis. 124:148, 1971; Chanda, P. K. et al., Virology 175:535, 1990); particles of viral or synthetic origin (e.g., Kofler, N. et al., J. Immunol. Methods. 192:25, 1996; Eldridge, J. H. et al., Sem. Hematol. 30:16, 1993; Falo, L. D., Jr. et al., Nature Med. 7:649, 1995); adjuvants (e.g., incomplete freund's advjuvant) (Warren, H. S., Vogel, F. R., and Chedid, L. A. Annu. Rev. Immunol. 4:369, 1986; Gupta, R. K. et al., Vaccine 11:293, 1993); liposomes (Reddy, R. et al., J. Immunol. 148:1585, 1992; Rock, K. L., Immunol. Today 17:131, 1996); or, particle-absorbed DNA (Ulmer, J. B. et al., Science 259:1745, 1993; Robinson, H. L., Hunt, L. A., and Webster, R. G., Vaccine 11:957, 1993; Shiver, J. W. et al., In: Concepts in vaccine development, Kaufmann, S. H. E., ed., p. 423, 1996; Cease, K. B., and Berzofsky, J. A., Annu. Rev. Immunol. 12:923, 1994 and Eldridge, J. H. et al., Sem. Hematol. 30:16, 1993), etc. Toxin-targeted delivery technologies, also known as receptor mediated targeting, such as those of Avant Immunotherapeutics, Inc. (Needham, Massachusetts) or attached to a stress protein, e.g., HSP 96 (Stressgen Biotechnologies Corp., Victoria, BC, Canada) can also be used.

Vaccines of the invention comprise nucleic acid mediated modalities. DNA or [00304] RNA encoding one or more of the peptides of the invention can be administered to a patient. This approach is described, for instance, in Wolff et. al., Science 247:1465 (1990) as well as U.S. Patent Nos. 5,580,859; 5,589,466; 5,804,566; 5,739,118; 5,736,524; 5,679,647; and, WO 98/04720. Examples of DNA-based delivery technologies include "naked DNA", facilitated (bupivicaine, polymers (e.g., PVP), peptide-mediated) delivery, cationic lipid complexes, and particle-mediated ("gene gun") or pressure-mediated delivery (see, e.g., U.S. Patent No. 5,922,687). Accordingly, peptide vaccines of the invention can be expressed by viral or bacterial vectors. Examples of expression vectors include attenuated viral hosts, such as vaccinia or fowlpox. For example, vaccinia virus is used as a vector to express nucleotide sequences that encode the peptides of the invention (e.g., MVA). Upon introduction into an acutely or chronically infected host or into a noninfected host, the recombinant vaccinia virus expresses the immunogenic peptide, and thereby elicits an immune response. Vaccinia vectors and methods useful in immunization protocols are described in, e.g., U.S. Patent No. 4,722,848. Another vector is BCG (Bacille Calmette Guerin). BCG vectors are described in Stover et al., Nature 351:456-460 (1991). A wide variety of other vectors useful for therapeutic administration or immunization of the peptides of the invention, e.g. adeno and adeno-associated virus vectors, alpha virus vectors, retroviral vectors, Salmonella typhi vectors, detoxified anthrax toxin vectors, and the like, are apparent to those skilled in the art from the description herein.

[00305] Furthermore, vaccines in accordance with the invention can comprise one or more peptides of the invention. Accordingly, a peptide can be present in a vaccine individually; alternatively, the peptide can exist as a homopolymer comprising multiple copies of the same peptide, or as a heteropolymer of various peptides. Polymers have the advantage of increased probability for immunological reaction and, where different peptide epitopes are used to make up the polymer, the ability to induce antibodies and/or T cells that react with different antigenic determinants of the antigen targeted for an immune response. The composition may be a naturally occurring region of an antigen or can be prepared, e.g., recombinantly or by chemical synthesis.

[00306] Carriers that can be used with vaccines of the invention are well known in the art, and include, e.g., thyroglobulin, albumins such as human serum albumin, tetanus toxoid, polyamino acids such as poly L-lysine, poly L-glutamic acid, influenza virus proteins,

hepatitis B virus core protein, and the like. The vaccines can contain a physiologically tolerable diluent such as water, or a saline solution, preferably phosphate buffered saline. Generally, the vaccines also include an adjuvant. Adjuvants such as incomplete Freund's adjuvant, aluminum phosphate, aluminum hydroxide, or alum are examples of materials well known in the art. Additionally, as disclosed herein, CTL responses can be primed by conjugating peptides of the invention to lipids, such as tripalmitoyl-S-glyceryl-cysteinyl-servine (P₃CSS).

- [00307] Upon immunization with a peptide composition in accordance with the invention, via injection (e.g., SC, ID, IM), aerosol, oral, transdermal, transmucosal, intrapleural, intrathecal, or other suitable routes, the immune system of the host responds to the vaccine by producing antibodies, CTLs and/or HTLs specific for the desired antigen. Consequently, the host becomes at least partially immune to subsequent exposure to the infectious agent, and thereby derives a prophylactic or therapeutic benefit.
- [00308] In certain embodiments, components that induce T cell responses are combined with components that induce antibody responses to the target antigen of interest. A preferred embodiment of such a composition comprises class I and class II epitopes in accordance with the invention. Alternatively, a composition comprises a class I and/or class II epitope in accordance with the invention, along with a PADRE® molecule (Epimmune, San Diego, CA).
- [00309] Vaccines of the invention can comprise antigen presenting cells, such as dendritic cells, as a vehicle to present peptides of the invention. For example, dendritic cells are transfected, e.g., with a minigene construct in accordance with the invention, in order to elicit immune responses. Minigenes are discussed in greater detail in a following section. Vaccine compositions can be created in vitro, following dendritic cell mobilization and harvesting, whereby loading of dendritic cells occurs in vitro.
- [00310] The vaccine compositions of the invention may also be used in combination with antiviral drugs such as interferon-α, or immune adjuvants such as IL-12, GM-CSF, etc.
- [00311] Preferably, the following principles are utilized when selecting epitope(s) and/or analogs for inclusion in a vaccine, either peptide-based or nucleic acid-based formulations. Exemplary variants that may be utilized in a vaccine to treat or prevent infectious agent-mediated disease are set out in Tables 6-9 and Figures 1A-4. Each of the following principles can be balanced in order to make the selection. When multiple epitopes are to be used in a vaccine, the epitopes may be, but need not be, contiguous in sequence in the

native antigen from which the epitopes are derived. Such multiple epitotes can refer to the order of epitopes within a peptide, or to the selection of epitopes that come from the same reagion, for use in either individual peptides or in a multi-epitopic peptide.

- 1.) Variants are selected which, upon administration, mimic immune responses that have been observed to be correlated with prevention or clearance of infectious disease. For HLA Class I, this generally includes 3-7 variants from at least one infectious agent or antigen thereof.
- 2.) Variants are selected that have the requisite binding affinity established to be correlated with immunogenicity: for HLA Class I an IC_{50} of 500 nM or less, or for Class II an IC_{50} of 1000 nM or less. For HLA Class I it is presently preferred to select a peptide having an IC_{50} of 200 nM or less, as this is believed to better correlate not only to induction of an immune response, but to *in vitro* tumor cell killing as well. For HLA A1 and A24, it is especially preferred to select a peptide having an IC_{50} of 100 nM or less.
- 3.) Supermotif bearing-variants, or a sufficient array of allele-specific motif-bearing variants, are selected to give broad population coverage. In general, it is preferable to have at least 80% population coverage. A Monte Carlo analysis, a statistical evaluation known in the art, can be employed to assess the breadth of population coverage.
- 4.) Of particular relevance are "nested epitopes." Nested epitopes occur where at least two epitopes overlap in a given peptide sequence. For example, a nested epitope can be a fragment of an antigen from a region that contains multiple epitopes that are overleapping, or one epitope that is completely encompassed by another, e.g., A2 peptides MAGE3.159 and MAGE3.160 are nested epitopes. A peptide comprising "transcendent nested epitopes" is a peptide that has both HLA class I and HLA class II epitopes in it. When providing nested epitopes, it is preferable to provide a sequence that has the greatest number of epitopes per provided sequence. Preferably, one avoids providing a peptide that is any longer than the amino terminus of the amino terminal epitope and the carboxyl terminus of the carboxyl terminal epitope in the peptide. When providing a sequence comprising nested epitopes, it is important to evaluate the sequence in order to insure that it does not have pathological or other deleterious biological properties; this is particularly relevant for vaccines directed to infectious organisms.
- 5.) If a protein with multiple epitopes or a polynucleotide (e.g., minigene) is created, an objective is to generate the smallest peptide that encompasses the epitopes of interest. This principle is similar, if not the same as that employed when selecting a peptide comprising nested epitopes. However, with an artificial peptide comprising multipe epitopes, the size minimization objective is balanced against the need to integrate any spacer sequences between epitopes in the polyepitopic protein. Spacer amino acid residues can be introduced to avoid junctional epitopes (an epitope recognized by the immune system, not present in the target antigen, and only created by the man-made juxtaposition of epitopes), or to facilitate cleavage between epitopes and thereby

enhance epitope presentation. Junctional epitopes are generally to be avoided because the recipient may generate an immune response to that non-native epitope. Of particular concern is a junctional epitope that is a "dominant epitope." A dominant epitope may lead to such a zealous response that immune responses to other epitopes are diminished or suppressed.

[00312] The principles are the same, except junctional epitopes applies to the sequences surrounding the epitope. One must also take care with other sequences in construct to avoid immune response.

T CELL PRIMING MATERIALS

- [00313] In some embodiments it may be desirable to include in the pharmaceutical compositions of the invention at least one component which primes cytotoxic T lymphocytes. Lipids have been identified as agents capable of facilitating the priming *in vitro* CTL response against viral antigens. For example, palmitic acid residues can be attached to the ε-and α- amino groups of a lysine residue and then linked to an immunogenic peptide. One or more linking moieties can be used such as Gly, Gly-Gly-, Ser, Ser-Ser, or the like. The lipidated peptide can then be administered directly in a micelle or particle, incorporated into a liposome, or emulsified in an adjuvant, *e.g.*, incomplete Freund's adjuvant. A preferred immunogenic composition comprises palmitic acid attached to ε- and α- amino groups of Lys via a linking moiety, *e.g.*, Ser-Ser, added to the amino terminus of an immunogenic peptide.
- [00314] In another embodiment of lipid-facilitated priming of CTL responses, *E. coli* lipoproteins, such as tripalmitoyl-S-glyceryl-cysteinyl-seryl-serine (P₃CSS) can be used to prime CTL when covalently attached to an appropriate peptide. (*See*, *e.g.*, Deres, *et al.*, *Nature* 342:561, 1989). Thus, peptides of the invention can be coupled to P₃CSS, and the lipopeptide administered to an individual to specifically prime a CTL response to the target antigen. Moreover, because the induction of neutralizing antibodies can also be primed with P₃CSS-conjugated epitopes, two such compositions can be combined to elicit both humoral and cell-mediated responses.

DENDRITIC CELLS PULSED WITH CTL AND/OR HTL PEPTIDES

[00315] An embodiment of a vaccine composition in accordance with the invention comprises ex vivo administration of a cocktail of epitope-bearing peptides to PBMC, or

isolated DC therefrom, from the patient's blood. A pharmaceutical to facilitate harvesting of DC can be used, such as ProgenipoietinTM (Monsanto, St. Louis, MO) or GM-CSF/IL-4. After pulsing the DC with peptides and prior to reinfusion into patients, the DC are washed to remove unbound peptides. In this embodiment, a vaccine comprises peptide-pulsed DCs which present the pulsed peptide epitopes in HLA molecules on their surfaces.

[00316] The DC can be pulsed ex vivo with a cocktail of peptides, some of which stimulate CTL responses to one or more antigens of interest, e.g., antigens from infectious agents such as HIV env, HIV pol, HIV gag, HIV vpu, HBV and/or the antigens in Tables 11-22, or otherwise described herein or know in the art. Optionally, a helper T cell (HTL) peptide such as PADRE®, can be included to facilitate the CTL response. Thus, a vaccine in accordance with the invention comprising epitopes from an infectious agent is used to treat or prevent disease mediated by these agents in patients. A vaccine can be used prior to, during, or following other therapies including, for example, antibiotic therepy, antiviral therapy (e.g., highly active antiretroviral therapy (HAART) in the case of HIV-AIDS), antibody therapy, cancer therapy, and adjunct thereapy, whereupon the vaccine provides descreased morbidity, increased disease free survival and overall survival in recipients.

DIAGNOSTIC AND PROGNOSTIC USES

[00317] In one embodiment of the invention, HLA class I and class II binding peptides can be used as reagents to evaluate an immune response. Preferably, the following principles are utilized when selecting a variant(s) for diagnostic, prognostic and similar uses. Potential principles include having the binding affinities described earlier, and/or matching the HLA-motif/supermotif of a peptide with the HLA-type of a patient.

[00318] The evaluated immune response can be induced by any immunogen. For example, the immunogen may result in the production of antigen-specific CTLs or HTLs that recognize the peptide epitope(s) employed as the reagent. Thus, a peptide of the invention may or may not be used as the immunogen. Assay systems that can be used for such analyses include tetramer-based protocols (e.g., DimerX technology (see, e.g., Science 274:94-99 (1996) and Proc. Natl. Acad. Sci. 95:7568-73 (1998)), staining for intracellular lymphokines, interferon release assays, or ELISPOT assays.

- [00319] For example, following exposure to a putative immunogen, a peptide of the invention can be used in a tetramer staining assay to assess peripheral blood mononuclear cells for the presence of any antigen-specific CTLs. The HLA-tetrameric complex is used to directly visualize antigen-specific CTLs and thereby determine the frequency of such antigen-specific CTLs in a sample of peripheral blood mononuclear cells (see, e.g., Ogg et al., Science 279:2103-2106, 1998; and Altman et al., Science 174:94-96, 1996).
- [00320] A tetramer reagent comprising a peptide of the invention is generated as follows: A peptide that binds to an HLA molecule is refolded in the presence of the corresponding HLA heavy chain and β_2 -microglobulin to generate a trimolecular complex. The complex is biotinylated at the carboxyl terminal end of the HLA heavy chain, at a site that was previously engineered into the protein. Tetramer formation is then induced by adding streptavidin. When fluorescently labeled streptavidin is used, the tetrameric complex is used to stain antigen-specific cells. The labeled cells are then readily identified, *e.g.*, by flow cytometry. Such procedures are used for diagnostic or prognostic purposes; the cells identified by the procedure can be used for therapeutic purposes.
- [00321] Peptides of the invention are also used as reagents to evaluate immune recall responses. (see, e.g., Bertoni et al., J. Clin. Invest. 100:503-513, 1997 and Penna et al., J. Exp. Med. 174:1565-1570, 1991.) For example, a PBMC sample from an individual expressing a disease-associated antigen (e.g. an antigen from an infectious agent) can be analyzed for the presence of antigen-specific CTLs or HTLs using specific peptides. A blood sample containing mononuclear cells may be evaluated by cultivating the PBMCs and stimulating the cells with a peptide of the invention. After an appropriate cultivation period, the expanded cell population may be analyzed, for example, for CTL or for HTL activity.
- [00322] Thus, the peptides can be used to evaluate the efficacy of a vaccine. PBMCs obtained from a patient vaccinated with an immunogen may be analyzed by methods such as those described herein. The patient is HLA typed, and peptide epitopes that are bound by the HLA molecule(s) present in that patient are selected for analysis. The immunogenicity of the vaccine is indicated by the presence of CTLs and/or HTLs directed to epitopes present in the vaccine.
- [00323] The peptides of the invention may also be used to make antibodies, using techniques well known in the art (see, e.g. CURRENT PROTOCOLS IN IMMUNOLOGY, Wiley/Greene, NY; and Antibodies A Laboratory Manual Harlow, Harlow and Lane, Cold

Spring Harbor Laboratory Press, 1989). Such antibodies are useful as reagents to determine the presence of disease-associated antigens. Antibodies in this category include those that recognize a peptide when bound by an HLA molecule, *i.e.*, antibodies that bind to a peptide-MHC complex.

ADMINISTRATION FOR THERAPEUTIC OR PROPHYLACTIC PURPOSES

[00324] The peptides and polynucleotides of the present invention, including cells and compositions comprising them, are useful for administration to mammals, particularly humans, to treat and/or prevent infection by an infectious agent such as HIV, HBV, HCV, HPV, Plasmodium falciparum and other agents described herein or known in the art. Vaccine compositions containing the peptides of the invention are administered to a patient infected with a particular infectious agent or to an individual susceptible to, or otherwise at risk for, infection with such an agent to elicit an immune response against antigens of that agent and thus enhance the patient's own immune response capabilities. Where susceptible individuals are identified prior to infection, the composition can be targeted to them, thus minimizing the need for administration to a larger population.

[00325] In therapeutic applications, peptide and/or nucleic acid compositions are administered to a patient in an amount sufficient to elicit an effective immune response to the infectious agent antigen and to thereby cure, arrest or slow symptoms and/or complications. An amount adequate to accomplish this is defined as "therapeutically effective dose." Amounts effective for this use will depend on, e.g., the particular composition administered, the manner of administration, the stage and severity of the disease being treated, the weight and general state of health of the patient, and the judgment of the prescribing physician.

[00326] The vaccine compositions of the invention can be used purely as prophylactic agents. Generally the dosage for an initial prophylactic immunization generally occurs in a unit dosage range where the lower value is about 1, 5, 50, 500, or 1000 μg of peptide and the higher value is about 10,000; 20,000; 30,000; or 50,000 μg of peptide. Dosage values for a human typically range from about 500 μg to about 50,000 μg of peptide per 70 kilogram patient. This is followed by boosting dosages of between about 1.0 μg to about 50,000 μg of peptide, administered at defined intervals from about four weeks to six months after the initial administration of vaccine. The immunogenicity of the vaccine may be assessed by measuring the specific activity of CTL and HTL obtained from a sample of the patient's blood.

[00327] As noted above, peptides comprising CTL and/or HTL epitopes of the invention induce immune responses when presented by HLA molecules and contacted with a CTL or HTL specific

for an epitope comprised by the peptide. The manner in which the peptide is contacted with the CTL or HTL is not critical to the invention. For instance, the peptide can be contacted with the CTL or HTL either *in vitro* or *in vivo*. If the contacting occurs *in vivo*, peptide can be administered directly, or in other forms/vehicles, *e.g.*, DNA vectors encoding one or more peptides, viral vectors encoding the peptide(s), liposomes, antigen presenting cells such as dendritic cells, and the like.

- [00328] Accordingly, for pharmaceutical compositions of the invention in the form of peptides or polypeptides, the peptides or polypeptides can be administered directly. Alternatively, the peptide/polypeptides can be administered indirectly presented on APCs, or as DNA encoding them. Furthermore, the peptides or DNA encoding them can be administered individually or as fusions of one or more peptide sequences.
- [00329] For therapeutic use, administration should generally begin at the first diagnosis of infectious agent-related disease. This is followed by boosting doses at least until symptoms are substantially abated and for a period thereafter. In chronic disease states, loading doses followed by boosting doses may be required.
- [00330] The dosage for an initial therapeutic immunization generally occurs in a unit dosage range where the lower value is about 1, 5, 50, 500, or 1,000 μg of peptide and the higher value is about 10,000; 20,000; 30,000; or 50,000 μg of peptide. Dosage values for a human typically range from about 500 μg to about 50,000 μg of peptide per 70 kilogram patient. Boosting dosages of between about 1.0 μg to about 50,000 μg of peptide, administered pursuant to a boosting regimen over weeks to months, can be administered depending upon the patient's response and condition. Patient response can be determined by measuring the specific activity of CTL and HTL obtained from the patient's blood.
- [00331] In certain embodiments, peptides and compositions of the present invention are used in serious disease states. In such cases, as a result of the minimal amounts of extraneous substances and the relative nontoxic nature of the peptides, it is possible and may be desirable to administer substantial excesses of these peptide compositions relative to these stated dosage amounts.
- [00332] For treatment of chronic disease, a representative dose is in the range disclosed above, namely where the lower value is about 1, 5, 50, 500, or 1,000 μg of peptide and the higher value is about 10,000; 20,000; 30,000; or 50,000 μg of peptide, preferably from about 500 μg to about 50,000 μg of peptide per 70 kilogram patient. Initial doses followed by boosting doses at established intervals, *e.g.*, from four weeks to six months, may be required, possibly for a prolonged period of time to effectively immunize an individual. In the case of chronic disease, administration should continue until at least clinical symptoms or laboratory tests indicate that the disease has been eliminated or substantially abated, and for a follow-up period thereafter. The dosages, routes of administration, and dose schedules are adjusted in accordance with methodologies known in the art.

[00333] The pharmaceutical compositions for therapeutic treatment are intended for parenteral, topical, oral, intrathecal, or local administration. Preferably, the pharmaceutical compositions are administered parentally, e.g., intravenously, subcutaneously, intradermally, or intramuscularly.

Thus, in a preferred embodiment the invention provides compositions for parenteral administration which comprise a solution of the immunogenic peptides dissolved or suspended in an acceptable carrier, preferably an aqueous carrier. A variety of aqueous carriers may be used, e.g., water, buffered water, 0.8% saline, 0.3% glycine, hyaluronic acid and the like. These compositions may be sterilized by conventional, well known sterilization techniques, or may be sterile filtered. The resulting aqueous solutions may be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile solution prior to administration. The compositions may contain pharmaceutically acceptable auxiliary substances or pharmaceutical excipients as may be required to approximate physiological conditions, such as pH-adjusting and buffering agents, tonicity adjusting agents, wetting agents, preservatives, and the like, for example, sodium acetate, sodium lactate, sodium chloride, potassium chloride, calcium chloride, sorbitan monolaurate, triethanolamine oleate, etc.

[00335] The concentration of peptides of the invention in the pharmaceutical formulations can vary widely, *i.e.*, from less than about 0.1%, usually at or at least about 2% to as much as 20% to 50% or more by weight, and will be selected primarily by fluid volumes, viscosities, *etc.*, in accordance with the particular mode of administration selected.

[00336] A human unit dose form of the peptide composition is typically included in a pharmaceutical composition that also comprises a human unit dose of an acceptable carrier, preferably an aqueous carrier, and is administered in a volume of fluid that is known by those of skill in the art to be used for administration of such compositions to humans (see, e.g., Remington's Pharmaceutical Sciences, 17th Edition, A. Gennaro, Editor, Mack Publishing Co., Easton, Pennsylvania, 1985).

[00337] The peptides of the invention can also be administered via liposomes, which serve to target the peptides to a particular tissue, such as lymphoid tissue, or to target selectively to infected cells, as well as to increase the half-life of the peptide composition. Liposomes include emulsions, foams, micelles, insoluble monolayers, liquid crystals, phospholipid dispersions, lamellar layers and the like. In these preparations, the peptide to be delivered is incorporated as part of a liposome, alone or in conjunction with a molecule which binds to a receptor prevalent among lymphoid cells (such as monoclonal antibodies which bind to the CD45 antigen) or with other therapeutic or immunogenic compositions. Thus, liposomes either filled or decorated with a desired peptide of the invention can be directed to the site of lymphoid cells, where the liposomes then deliver the peptide compositions. Liposomes for use in accordance with the invention are formed from standard vesicle-forming lipids, which generally include neutral and negatively

charged phospholipids and a sterol, such as cholesterol. The selection of lipids is generally guided by consideration of, e.g., liposome size, acid lability and stability of the liposomes in the blood stream. A variety of methods are available for preparing liposomes, as described in, e.g., Szoka, et al., Ann. Rev. Biophys. Bioeng. 9:467 (1980), and U.S. Patent Nos. 4,235,871, 4,501,728, 4,837,028, and 5,019,369.

[00338] For targeting compositions of the invention to cells of the immune system, a ligand can be incorporated into the liposome, e.g., antibodies or fragments thereof specific for cell surface determinants of the desired immune system cells. A liposome suspension containing a peptide may be administered intravenously, locally, topically, etc. in a dose which varies according to, inter alia, the manner of administration, the peptide being delivered, and the stage of the disease being treated.

[00339] For solid compositions, conventional nontoxic solid carriers may be used which include, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharin, talcum, cellulose, glucose, sucrose, magnesium carbonate, and the like. For oral administration, a pharmaceutically acceptable nontoxic composition is formed by incorporating any of the normally employed excipients, such as those carriers previously listed, and generally 10-95% of active ingredient, that is, one or more peptides of the invention, often at a concentration of 25%-75%.

[00340] For aerosol administration, the immunogenic peptides are preferably supplied in finely divided form, along with a surfactant and propellant. Typical percentages of peptides are 0.01%-20% by weight, often 1%-10%. The surfactant must, of course, be pharmaceutically acceptable, and preferably soluble in the propellant. Representative of such agents are the esters or partial esters of fatty acids containing from 6 to 22 carbon atoms, such as caproic, octanoic, lauric, palmitic, stearic, linoleic, linolenic, olesteric and oleic acids with an aliphatic polyhydric alcohol or its cyclic anhydride. Mixed esters, such as mixed or natural glycerides may be employed. The surfactant may constitute 0.1%-20% by weight of the composition, preferably 0.25-5%. The balance of the composition is ordinarily propellant, although an atomizer may be used in which no propellant is necessary and other percentages are adjusted accordingly. A carrier can also be included, e.g., lecithin for intranasal delivery.

[00341] Antigenic peptides of the invention have been used to elicit a CTL and/or HTL response ex vivo, as well. The resulting CTLs or HTLs can be used to treat chronic infections, or tumors in patients that do not respond to other conventional forms of therapy, or who do not respond to a therapeutic peptide or nucleic acid vaccine in accordance with the invention. Ex vivo CTL or HTL responses to a particular antigen (infectious or tumor-associated) are induced by incubating in tissue culture the patient's, or genetically compatible, CTL or HTL precursor cells together with a source of antigen-presenting cells (APC), such as dendritic cells, and the appropriate immunogenic

peptide. After an appropriate incubation time (typically about 7-28 days), in which the precursor cells are activated and expanded into effector cells, the cells are infused back into the patient, where they will destroy (CTL) or facilitate destruction (HTL) of their specific target cell (an infected cell or a tumor cell).

KITS

- [00342] The peptide and nucleic acid compositions of this invention can be provided in kit form together with instructions for vaccine administration. Typically the kit would include desired composition(s) of the invention in a container, preferably in unit dosage form and instructions for administration. For example, a kit would include an APC, such as a dendritic cell, previously exposed to and now presenting peptides of the invention in a container, preferably in unit dosage form together with instructions for administration. An alternative kit would include a minigene construct with desired nucleic acids of the invention in a container, preferably in unit dosage form together with instructions for administration. Lymphokines such as IL-2 or IL-12 may also be included in the kit. Other kit components that may also be desirable include, for example, a sterile syringe, booster dosages, and other desired excipients.
- [00343] The invention will be described in greater detail by way of specific examples. The following examples are offered for illustrative purposes, and are not intended to limit the invention in any manner. Those of skill in the art will readily recognize a variety of non-critical parameters that can be changed or modified to yield alternative embodiments in accordance with the invention.

EXAMPLES

EXAMPLE 1. HLA CLASS I AND CLASS II BINDING ASSAYS

- [00344] The following example of peptide binding to HLA molecules demonstrates quantification of binding affinities of HLA class I and class II peptides. Binding assays can be performed with peptides that are either motif-bearing or not motif-bearing.
- [00345] Cell lysates were prepared and HLA molecules purified in accordance with disclosed protocols (Sidney et al., Current Protocols in Immunology 18.3.1 (1998); Sidney, et al., J. Immunol. 154:247 (1995); Sette, et al., Mol. Immunol. 31:813 (1994)).

The cell lines used as sources of HLA molecules and the antibodies used for the extraction of the HLA molecules from the cell lysates are also described in these publications and are well known in the art.

- [00346] Epstein-Barr virus (EBV)-transformed homozygous cell lines, fibroblasts, CIR, or 721.221-transfectants were used as sources of HLA class I molecules. These cells were cultured in RPMI 1640 medium supplemented with 2mM L-glutamine (GIBCO, Grand Island, NY), 50μM 2-ME, 100μg/ml of streptomycin, 100U/ml of penicillin (Irvine Scientific) and 10% heat-inactivated FCS (Irvine Scientific, Santa Ana, CA).
- [00347] Cell lysates were prepared as follows. Briefly, cells were lysed at a concentration of 10⁸ cells/ml in 50 mM Tris-HCl, pH 8.5, containing 1% Nonidet P-40 (Fluka Biochemika, Buchs, Switzerland), 150 mM NaCl, 5 mM EDTA, and 2 mM PMSF. Lysates were cleared of debris and nuclei by centrifugation at 15,000 x g for 30min.
- Were passed twice through two pre-columns of inactivated Sepharose CL4-B and protein A-Sepharose. Next, the lysate was passed over a column of Sepharose CL4-B beads coupled to an appropriate antibody. The anti-HLA column was then washed with 10-column volumes of 10mM Tris-HCL, pH 8.0, in 1% NP-40, PBS, 2-column volumes of PBS, and 2-column volumes of PBS containing 0.4% n-octylglucoside. Finally, MHC molecules were eluted with 50mM diethylamine in 0.15M NaCl containing 0.4% n-octylglucoside, pH 11.5. A 1/25 volume of 2.0M Tris, pH 6.8, was added to the eluate to reduce the pH to ~8.0. Eluates were then concentrated by centrifugation in Centriprep 30 concentrators at 2000 rpm (Amicon, Beverly, MA). Protein content was evaluated by a BCA protein assay (Pierce Chemical Co., Rockford, IL) and confirmed by SDS-PAGE.
- [00349] A detailed description of the protocol utilized to measure the binding of peptides to Class I and Class II MHC has been published (Sette *et al.*, *Mol. Immunol.* 31:813, 1994; Sidney *et al.*, in *Current Protocols in Immunology*, Margulies, Ed., John Wiley & Sons, New York, Section 18.3, 1998). Briefly, purified MHC molecules (5 to 500nM) were incubated with various unlabeled peptide inhibitors and 1-10nM ¹²⁵I-radiolabeled probe peptides for 48h in PBS containing 0.05% Nonidet P-40 (NP40) (or 20% w/v digitonin for H-2 IA assays) in the presence of a protease inhibitor cocktail. The final concentrations of protease inhibitors (each from CalBioChem, La Jolla, CA) were 1 mM PMSF, 1.3 nM 1.10 phenanthroline, 73 μM pepstatin A, 8mM EDTA, 6mM N-ethylmaleimide (for Class II assays), and 200 μM N alpha-p-tosyl-L-lysine chloromethyl ketone (TLCK). All assays

were performed at pH 7.0 with the exception of DRB1*0301, which was performed at pH 4.5, and DRB1*1601 (DR2w21β₁) and DRB4*0101 (DRw53), which were performed at pH 5.0. pH was adjusted as described elsewhere (see Sidney et al., in Current Protocols in Immunology, Margulies, Ed., John Wiley & Sons, New York, Section 18.3, 1998).

- [00350] Following incubation, MHC-peptide complexes were separated from free peptide by gel filtration on 7.8 mm x 15 cm TSK200 columns (TosoHaas 16215, Montgomeryville, PA), eluted at 1.2 mls/min with PBS pH 6.5 containing 0.5% NP40 and 0.1% NaN₃. Because the large size of the radiolabeled peptide used for the DRB1*1501 (DR2w2β₁) assay makes separation of bound from unbound peaks more difficult under these conditions, all DRB1*1501 (DR2w2β₁) assays were performed using a 7.8mm x 30cm TSK2000 column eluted at 0.6 mls/min. The eluate from the TSK columns was passed through a Beckman 170 radioisotope detector, and radioactivity was plotted and integrated using a Hewlett-Packard 3396A integrator, and the fraction of peptide bound was determined.
- [00351] Radiolabeled peptides were iodinated using the chloramine-T method. Representative radiolabeled probe peptides utilized in each assay, and its assay specific IC₅₀ nM, are known in the art. Typically, in preliminary experiments, each MHC preparation was titered in the presence of fixed amounts of radiolabeled peptides to determine the concentration of HLA molecules necessary to bind 10-20% of the total radioactivity. All subsequent inhibition and direct binding assays were performed using these HLA concentrations.
- Since under these conditions [label]<[HLA] and IC₅₀≥[HLA], the measured IC₅₀ values are reasonable approximations of the true K_D values. Peptide inhibitors are typically tested at concentrations ranging from 120 μg/ml to 1.2 ng/ml, and are tested in two to four completely independent experiments. To allow comparison of the data obtained in different experiments, a relative binding figure is calculated for each peptide by dividing the IC₅₀ of a positive control for inhibition by the IC₅₀ for each tested peptide (typically unlabeled versions of the radiolabeled probe peptide). For inter-experiment comparisons, relative binding values are compiled. These values can subsequently be converted back into IC₅₀ nM values by dividing the IC₅₀ nM of the positive controls for inhibition by the relative binding of the peptide of interest. This method of data compilation has proven to be the most accurate and consistent for comparing peptides that have been tested on different days, or with different lots of purified MHC.

- Because the antibody used for HLA-DR purification (LB3.1) is α -chain specific, [00353] β_1 molecules are not separated from β_3 (and/or β_4 and β_5) molecules. The β_1 specificity of the binding assay is obvious in the cases of DRB1*0101 (DR1), DRB1*0802 (DR8w2), and DRB1*0803 (DR8w3), where no β₃ is expressed. It has also been demonstrated for DRB1*0301 (DR3) and DRB3*0101 (DR52a), DRB1*0401 (DR4w4), DRB1*0404 (DR4w14), DRB1*0405 (DR4w15), DRB1*1101 (DR5), DRB1*1201 (DR5w12), DRB1*1302 (DR6w19) and DRB1*0701 (DR7). The problem of β chain specificity for DRB5*0101 $(DR2w2\beta_2)$, DRB1*1601 $(DR2w21\beta_1)$, $(DR2w2\beta_1)$, DRB1*1501 DRB5*0201 (DR51Dw21), and DRB4*0101 (DRw53) assays is circumvented by the use of fibroblasts. Development and validation of assays with regard to DRB molecule specificity have been described previously (see, e.g., Southwood et al., J. Immunol. 160:3363-3373, 1998).
- [00354] Binding assays as outlined above may be used to analyze supermotif and/or motifbearing epitopes.

EXAMPLE 2. RECOGNITION OF VARIANT PEPTIDES BY CTL DERIVED FROM DNA IMMUNIZATION

- Variants corresponding to five HLA-A2 and -A3 restricted epitopes from 167 HIV varianst were identified and synthesized. These represented all the complete sequences in the Los Alamos database at the time (116 strains), as well as 51 complete clade C sequences from Botswana, and included 22 subtype B and 62 subtype C sequences. These peptides were then characterized with regard to MHC binding, variant distribution, and immunogenicity. To measure immunogenicity, HLA-A2/K^b or HLA-A11/K^b transgenic mice were immunized with the epitopes encoded in a DNA based format (). Eleven days after immunization, splenocytes were restimulated with either the epitope corresponding to the epitope encoded by the DNA (parent) or each of the variant peptides. After 6 days in culture, IFN-γ secretion was measured in response to the peptide used to stimulate each culture.
- [00356] The data for these epitopes are shown in Figure 1. The HLA-A2-restricted epitope corresponding to the Env 134 epitope (KLTPLCVTL, SEQ ID NO: 9; Figure 1A) used as the immunogen was the form observed most often (134/167). All single anchor variants

were recognized to approximately the same extent as the parent peptide. Many of the single non-anchor variants (9/13) were also recognized within 10-fold of the parent peptide. Conservative substitutions (R and Q for K; see Table 4) at position 1 (P1) were tolerated, while the non-conservative substitution (E for K; see Table 4) lowered binding and eliminated recognition. Three P4 variants were observed. Two of these (F or S for P) were recognized within 10-fold of the recognition of the parent peptide, while one substitution (Q for P) completely eliminated recognition. The binding for these peptides was not significantly different from the parent peptide, indicating that this residue may be involved in TCR recognition. Both the conservative (F for L) and non-conservative (R for L) substitutions seen at P5 completely abrogated recognition, indicating that this residue is important in TCR recognition. Finally, one substitution at P8 (I for V), and four substitutions at P9 show little effect on recognition. None of the variants with multiple substitutions were recognized, although this may be due to the poor binding of these peptides.

[00357] The Gag 386 sequence utilized as the immunogen was the second most common form (VLAEAMSQV, SEQ ID NO: 10), present in 54 strains (Figure 1B). The most prevalent variant, differing by a single tolerated C terminal anchor residue (V to A; 67 strains), was recognized equally to the parent epitope by CTL raised against the parent, as were the remaining single-anchor variants. Single substitutions were also tolerated at the non-anchor positions, P1 (I for V) and P8 (R, K, or H for Q). Only the P7 variant (G for S), probably a TCR contact residue, was not recognized.

[00358] Many of the multiple variants for Gag 386 were also recognized by CTL raised against the parent peptide. All the variants with multiple changes combined a change of V to A or T at the C terminus with 1-3 additional substitutions. Two variants with N terminal changes (V to A or I) were observed. The non-conservative A substitution was not recognized, while the conservative I substitution was. A double variant with a conservative substitution at P3 (A to G) was not recognized, implicating P3 in TCR recognition. Double variants with conservative changes at position 8 (Q to R, K, or H) were not well recognized, although the variants with single changes at the same positions were recognized. The variant combining a non-conservative A residue at position 8 with A at the C terminus was recognized as well as the parent. Equally surprising was the observation that all the variants with 3 or 4 substitutions were recognized within 10-fold of the parent peptide.

[00359] The parent form of the HLA-A2-restricted epitope, Vpr 62 (RILQQLLFI, SEQ ID NO: 11; Figure 1C) was the most common form observed (86/167). Seven well-tolerated single anchor substitutions, 4 P2 and 3 C terminal, were also observed, accounting for most of the remaining variants (47/167). Single substitutions were, in general, also well tolerated. The single exception was the non-conservative substitution (P for L) at P6, while an M for L substitution at the same site was well tolerated. Binding was not affected for either variant, indicating that the reduction in activity is due to a change in a contact residue. Most variants with multiple changes also showed recognition to approximately the same extent as the parent. Several variants however did show reduced recognition. The variant with changes at both anchors (I to T at P2 and I to T at P9) had reduced binding (IC₅₀ of 9700), and recognition of the peptide was reduced, although not lost completely. Two variants with Q to H changes at P5, in combination with anchor residue changes (I to M at P2 and I to A at P9), exhibited greatly reduced recognition although binding was not affected. Other changes at P5 (Q to R or L at P5) reduced recognition only slightly.

[00360] The HLA-A3/11-restricted epitope, Pol 98 (Figure 1D), represented the most diverse epitope in terms of the number of variant epitopes identified. The peptide encoded in the DNA was represented in only 18 out of 167 strains. Approximately a third of the peptides identified at that position (49 out of 167) did not have recognizable A3/A11 motifs. The most common variant (30 strains) differed from the parent peptide at 3 residues (VSIKVGGQIK, SEQ ID NO: 12), but was recognized within 10-fold of the parent peptide. Two variants with conservative changes at anchor residues were both recognized, although the T to A substitution at P2 resulted in a 10-fold reduction in recognition of the variant peptide. All peptides with single changes in non-anchor positions were also recognized, although the P5 variant (G to E) exhibited a decrease in recognition. As the binding was not affected, this probably indicates involvement in T cell recognition.

[00361] Peptides with two changes showed mixed results. In general, peptides with a V substitution at position 3, in combination with another substitution were recognized to the same extent as the corresponding single substitution, indicating the V substitution was tolerated well and is not a TCR contact residue. Combinations including the P2 anchor residue (T to A or N) were not recognized, although the binding of these peptides was also low. Variants with 3 substitutions were generally not recognized well. Two exceptions

with very conservative substitutions were noted (Figure 1D). CTL were unable to recognize peptides with four or more substitutions.

- [00362] The HLA-A3/11- restricted Env 47 epitope (Figure 1E; VTVYYGVPVWK, SEQ ID NO: 13) was highly conserved, with only 9 variants identified. The most common form observed was the parent peptide (99 strains), while the second most common form, a single anchor substitution observed in 40 strains, was recognized to the same extent as the parent. All the variants were recognized within 10-fold of the parent epitope.
- [00363] Taken together, these data show trends towards promiscuous recognition of variant peptides by CTL generated from immunization with a single peptide. In general, changes that disrupted binding also decreased recognition. Recognition was also affected by the position of the change, with potential TCR contact residues (P3-7) exerting a greater effect on recognition than other residues. In general, conservative residue changes were more widely tolerated than were non-conservative changes. Recognition was also dependent on the number of changes, with progressively lower recognition with a greater number of changes.
- [00364] Recognition after multiple restimulations The observed recognition of variant peptides by CTL raised against the parent peptide might be due to either promiscuous recognition at the level of a single TCR or simply a mixture of TCRs against the immunizing peptide which are each able to recognize subtly different peptides. To distinguish between these two possibilities, Env 134- or Gag 386-specific T cell lines were generated by stimulating five times with the immunizing peptide, and then tested for recognition of a partial panel of variant peptides. These T cell lines were also characterized for Vβ TCR usage against a panel of antibodies predicted to react with the TCR of the mouse strains utilized for these experiments.
- [00365] The data for these peptide-specific lines are shown in Table 5. Because the SU is a measure of the number of cells needed to secrete a defined amount of IFN-γ, a higher SU value would correspond to an enrichment of IFN-γ producing cells. A comparison of one and five peptide stimulations indeed shows an enrichment of CTL specific for the immunizing peptide for both of the peptide lines generated (Table 5A and 5B, first line). The Gag 386 line (Table 5A) also demonstrated increased recognition of all the variant peptides measured except one peptide (ILAEAMSKA, SEQ ID NO: 14) that was never

recognized. The Env 134 line also demonstrated enrichment for CTL able to recognize several of the variant peptides (Table 5B).

[00366] To further characterize these lines, we examined them for Vβ usage, utilizing a panel of commercially available antibodies available for mouse TCR Vβ 2-14. To determine background levels for the various TCR Vβ molecules, primary splenocytes from mice that had been immunized with EP HIV-1090 were also examined. The results for the Gag 386 line are shown in Figure 2A. After a single stimulation with the parent peptide, the Gag 386 line showed a mixture of TCR positive populations, including Vβ 3, 5, and 14. After 5 stimulations, those populations had been reduced to background levels, and approximately 50% of the CD8+ cells expressed the Vβ 6 TCR. The Env 134 line showed a similar pattern of multiple TCR positive populations after a single round of stimulation with reduction to background levels after 5 stimulations (data not shown). However, no single Vβ usage significantly above background could be demonstrated, probably due to lack of the relevant TCR Vβ antibody.

[00367] Both lines were also characterized with regard to the affinity of certain of the variant peptides by titrating the variant peptides examined above (Table 5A and 5B). The data for both the Gag 386 and Env 134 lines are shown in Figure 2B. For the Gag 386 line, the parent peptide along with two single anchor variants (VLAEAMSQI, SEQ ID NO: 15, and VLAEAMSQA, SEQ ID NO: 16) showed the highest affinity. Four other peptides demonstrated lower affinity, but still produced IFN-γ in response to higher peptide concentrations. A single peptide (ILAEAMSKA, SEQ ID NO: 14) was not recognized.

[00368] As expected, the parent peptide, which was used to generate the Env 134 line, showed the highest affinity for the TCR. The other 2 variant peptides, KITPLCVTL (SEQ ID NO: 18) and QLTPLCVTL (SEQ ID NO: 19), also demonstrated higher affinity, but reduced from the parent peptide by approximately 10-fold and 100-fold, respectively. It was notable that only at the highest peptide concentration examined (1 μg/ml) was any IFN-γ secretion detected for five of the peptides (QITPLCVTL, SEQ ID NO: 20, ELTPLCVTL, SEQ ID NO: 21, KLTPFCVTL, SEQ ID NO: 22, KLTPLCVIL, SEQ ID NO: 23, and KLTPLCVPL, SEQ ID NO: 24). These five peptides showed little or no enrichment of CTL able to recognize them, and exhibited the lowest activity as measured by SU after five restimulations (see Table 5B).

[00369] In summary, these cell lines seem to consist of a narrow, possibly single, TCR population. This TCR population recognizes the parent peptide with the highest affinity,

but is also able to recognize a number of other variant peptides with equal or lesser affinity.

[00370] Recognition of variant peptides by CTL derived from an HIV infected patient.

[00371] To determine if the same immunological conservation was observed in natural infections, we identified an HIV-infected individual expressing the HLA-A3 allele. The HIV strain and subtype with which this patient was infected is unknown. We had previously shown that T cells from this individual responded to the HLA-A3 restricted epitopes Pol 98 and Env 47. PBL from this patient were examined in an ELISPOT assay to determine if they also showed the capacity for broad cross-reactivity. The data are shown in Figure 3. Although the actual peptide represented in the HIV strain with which this individual is infected is unknown, we observed recognition of a large number of the variant peptides for both Pol 98 (Figure 3A) and Env 47 (Figure 3B). The recognition patterns were remarkably similar for the mouse and patient data (compare Figure 1 and Figure 3), although the mouse expressed a transgene for HLA-A11 and the patient was HLA-A3.

[00372] Prediction of Immunological Conservation. We had observed that the variant peptides that were recognized by CTL raised against the parent epitope had amino acid substitutions that followed previous observations. For example, the anchor residue changes that were tolerated in the variant peptides were also described as anchors that to define the respective HLA supertypes (). In general, conservative substitutions were tolerated at non-anchor residues, while non-conservative substitutions were less well tolerated. These followed closely the prediction model used to identify heteroclitic analogs (Tangri et al).

[00373] Based on these observations, we designed a computer program to predict immunological conservation. For anchor positions, this program utilized the conserved anchor residues described for the A2, A3, and B7 supertypes. For non-anchor positions only conservative substitutions, as defined in Tangri et.al. (), were allowed. All substitutions at non-anchor positions were analyzed independently and all conservative substitutions were allowed regardless of the number of substitutions. Finally, the position of the substitution was not factored into analysis. Each variant was compared with the parent epitope, and its ability to be recognized was predicted as either positive or negative.

[00374] The first sets of epitopes to be evaluated by this program were the five HIV epitopes and variants previously described. For the Env 134 epitope, the program predicted that 13 of the variant peptides should be immunologically conserved, while 6 should not be recognized. Comparison of the observed immunological data with the prediction showed that the program predicted correctly for 14 of the peptides and incorrectly for 5. Of the incorrect predictions, in two cases the program predicted negative results for peptides that were recognized, while in 3 cases the program predicted positive results for peptides that were not recognized. A similar analysis was performed for all five peptides. Of 101 total variant peptides, 68 were correctly identified (67%). The discordant data were fairly evenly split between peptides incorrectly predicted negative (15) and those incorrectly predicted positive (18).

[00375] As noted previously, the more substitutions present in a variant peptide, the lower the likelihood of its immunogenicity. Since the prediction program treated all substitutions independently, and did not take into account the number of substitutions, we hypothesized that prediction of single substitutions would be more accurate. Indeed, the immunogenicity of 38 of 47 single substitution variants (80%) was correctly predicted.

[00376] With the limitations of the program in mind, it is useful to predict the recognition of the variants for a package of HLA-A2, -A3, and -B7 supertype epitopes. These epitopes had been identified as being well conserved in Clade B variants. When comparing the conservation of this group of epitopes based on sequence identity versus immunological conservation, it is interesting to note that the predicted recognition gains taking into account immunological conservation are significant (Table 6).

[00377] This particular group of 21 epitopes was selected based on their identity conservation in Clade B HIV sequences, with conservation across HIV clades as a secondary consideration. Because of this criteria, the form of epitope chosen as the parent peptide was not the most common variant (e.g. Gag 386, Gag 271, Pol 98). In some cases (e.g., see Gag 386 data), the "parent" epitope and the most common variant were recognized to the same extent. However, in some cases the selection of epitope to include as the "parent" epitope was predicted to make a difference in the immunological conservation. An example of this was the Gag 271 epitope (Figure 4). The variant most commonly seen in clade B sequences was the MTNNPPIPV form (SEQ ID NO: 25), while the most common form of the epitope was MTSNPPIPV (SEQ ID NO: 26). Not all amino acids are considered equal to each other in their ability to substitute (Tangri). For example,

asparagine (N) is considered a conservative substitution for serine (S), while the opposite substitution in only considered semi-conserved. When the program calculated immunological conservation using the MTNNPPIPV peptide (SEQ ID NO: 25) as the parent peptide, only two variants were predicted to be immunogenic. However, when the immunological conservation was predicted using the MTSNPPIPV peptide (SEQ ID NO: 26), most of the variants were predicted to be recognized (Figure 4). This prediction was tested using HLA-A2 transgenic mice. The results show that if the MTSNPPIPV form (SEQ ID NO: 26) of the peptide was utilized in vaccines, approximately 152 of 167 variants would be recognized, while if the MTNNPPIPV form (SEQ ID NO: 25) of the epitope was utilized, only 39 of 167 variants would be recognized. This has important implications in epitope selection for vaccine development, and epitope performance can be predicted.

EXAMPLE 3. A PADRE® MOLECULE AS A HELPER EPITOPE FOR ENHANCEMENT OF CTL INDUCTION

[00378] There is increasing evidence that HTL activity is critical for the induction of long-lasting CTL responses (Livingston et al. J. Immunol 162:3088-3095 (1999); Walter et al., New Engl. J. Med. 333:1038-1044 (1995); Hu et al., J. Exp. Med. 177:1681-1690 (1993)). Therefore, one or more peptides that bind to HLA class II molecules and stimulate HTLs can be used in accordance with the invention. Accordingly, a preferred embodiment of a vaccine includes a molecule from the PADRE® family of universal T helper cell epitopes (HTL) that target most DR molecules in a manner designed to stimulate helper T cells. For instance, a pan-DR-binding epitope peptide having the formula: aKXVAAZTLKAAa, where "X" is either cyclohexylalanine, phenylalanine, or tyrosine; "Z" is either tryptophan, tyrosine, histidine or asparagine; and "a" is either D-alanine or L-alanine (SEQ ID NO:29), has been found to bind to most HLA-DR alleles, and to stimulate the response of T helper lymphocytes from most individuals, regardless of their HLA type.

[00379] A particularly preferred PADRE molecule is a synthetic peptide, aKXVAAWTLKAAa SEQ ID NO: 28 (a = D-alanine, X = cyclohexylalanine), containing non-natural amino acids, specifically engineered to maximize both HLA-DR binding capacity and induction of T cell immune responses.

- Alternative preferred PADRE® molecules are the peptides, aKFVAAWTLKAAa [00380] (SEQ ID NO: 29), aKYVAAWTLKAAa (SEQ ID NO: 30), aKFVAAYTLKAAa (SEQ ID NO: 31), aKXVAAYTLKAAa (SEQ ID NO: 32), aKYVAAYTLKAAa (SEQ ID NO: 33), aKFVAAHTLKAAa (SEQ ID NO: 34), aKXVAAHTLKAAa (SEQ ID NO: 35), aKYVAAHTLKAAa (SEO ID NO: 36), aKFVAANTLKAAa (SEO ID NO: 37), aKXVAANTLKAAa (SEQ ID NO: 38), aKYVAANTLKAAa (SEQ ID NO: 39), AKXVAAWTLKAAA (SEQ ID NO: [[30]] 40), AKFVAAWTLKAAA (SEQ ID NO: [[31]] 41), AKYVAAWTLKAAA (SEQ ID NO:[[32]] 42), AKFVAAYTLKAAA (SEQ ID NO:[[33]] 43), AKXVAAYTLKAAA (SEQ ID NO:[[34]] 44), AKYVAAYTLKAAA AKFVAAHTLKAAA (SEQ ID ID NO: [[35]] 45), NO:[[36]] AKXVAAHTLKAAA (SEQ ID NO:[[37]] 47), AKYVAAHTLKAAA (SEQ ID NO:[[38]] 48), AKFVAANTLKAAA (SEQ ID NO:[[39]] 49), AKXVAANTLKAAA (SEQ ID NO:[[40]] 50), AKYVAANTLKAAA (SEQ ID NO:[[41]] 51) (a = D-alanine, X = cyclohexylalanine).
- [00381] In a preferred embodiment, the PADRE® peptide is amidated. For example, a particularly preferred amidated embodiment of a PADRE® molecule is conventionally written aKXVAAWTLKAAa-NH₂.
- [00382] Competitive inhibition assays with purified HLA-DR molecules demonstrated that the PADRE® molecule aKXVAAWTLKAAa-NH₂ binds with high or intermediate affinity (IC₅₀ ≤1,000 nM) to 15 out of 16 of the most prevalent HLA-DR molecules ((Kawashima *et al.*, *Human Immunology* 59:1-14 (1998); Alexander *et al.*, *Immunity* 1:751-761 (1994)). A comparison of the DR binding capacity of PADRE® and tetanus toxoid (TT) peptide 830-843, a "universal" epitope has been published (Panina-Bordignon *et al.*, *Eur. J. Immunology* 19:2237-2242 (1989)). The TT 830-843 peptide bound to only seven of 16 DR molecules tested, while PADRE® bound 15 of 16. At least 1 of the 15 DR molecules that bind PADRE® is predicted to be present in >95% of all humans. Therefore, this PADRE® molecule is anticipated to induce an HTL response in virtually all patients, despite the extensive polymorphism of HLA-DR molecules in the human population.
- [00383] PADRE® has been specifically engineered for optimal immunogenicity for human T cells. Representative data from *in vitro* primary immunizations of normal human T cells with TT 830-843 antigen and the PADRE® molecule aKXVAAWTLKAAa-NH₂ are shown in Figure 1. Peripheral blood mononuclear cells (PBMC) from three normal donors

were stimulated with the peptides *in vitro*. Following the third round of stimulation, it was observed that PADRE[®] generated significant primary T cell responses for all three donors as measured in a standard T cell proliferation assay. With the PADRE[®] peptide, the 10,000 cpm proliferation level was generally reached with 10 to 100 ng/ml of antigen. In contrast, TT 830-843 antigen generated responses for only 2 out of 3 of the individuals tested. Responses approaching the 10,000 cpm range were reached with about 10,000 ng/ml of antigen. In this respect, it was noted that PADRE[®] was, on a molar basis, about 100-fold more potent than TT 830-843 antigen for activation of T cell responses.

Early data from a phase I/II investigator-sponsored trial, conducted at the [00384] University of Leiden (C.J.M. Melief), support the principle that the PADRE® molecule aKXVAAWTLKAAa (SEQ ID NO: 28), possibly the amidated aKXVAAWTLKAAa -NH₂, is highly immunogenic in humans (Ressing et al., J. Immunother. 23(2):255-66 (2000)). In this trial, a PADRE® molecule was co-emulsified with various human papilloma virus (HPV)-derived CTL epitopes and was injected into patients with recurrent or residual cervical carcinoma. However, because of the late stage of carcinoma with the study patients, it was expected that these patients were immunocompromised. patients' immunocompromised status was demonstrated by their low frequency of influenza virus-specific CTL, reduced levels of CD3 expression, and low incidence of proliferative recall responses after in vitro stimulation with conventional antigens. Thus, no efficacy was anticipated in the University of Leiden trial, rather the goal of that trial was essentially to evaluate safety. Safety was, in fact, demonstrated. In addition to a favorable safety profile, PADRE® T cell reactivity was detected in four of 12 patients (Figure 2) in spite of the reduced immune competence of these patients.

[00385] Thus, the PADRE[®] peptide component(s) of the vaccine bind with broad specificity to multiple allelic forms of HLA-DR molecules. Moreover, PADRE[®] peptide component(s) bind with high affinity (IC₅₀ \leq 1000 nM), i.e., at a level of affinity correlated with being immunogenic for HLA Class II restricted T cells. The *in vivo* administration of PADRE[®] peptide(s) stimulates the proliferation of HTL in normal humans as well as patient populations.

[00386] One or more PADRE® peptide(s) may be included in a composition, e.g., a vaccine, comprising one or more peptides, either as an individual peptide(s), fused to one or more variant peptides, or both.

EXAMPLE 4. CTL RECOGNITION OF ENDOGENOUS PROCESSED ANTIGENS AFTER PRIMING

[00387] This example determines that CTL induced by native or analoged peptide epitopes recognize endogenously synthesized, *i.e.*, native antigens.

[00388] Effector cells isolated from transgenic mice that are immunized with peptide epitopes are re-stimulated *in vitro* using peptide-coated stimulator cells. Six days later, effector cells are assayed for cytotoxicity and the cell lines that contain peptide-specific cytotoxic activity are further re-stimulated. An additional six days later, these cell lines are tested for cytotoxic activity on ⁵¹Cr labeled Jurkat-A2.1/K^b target cells in the absence or presence of peptide, and also tested on ⁵¹Cr labeled target cells bearing the endogenously synthesized antigen, *i.e.* cells that are stably transfected with HIV expression vectors.

[00389] The result will demonstrate that CTL lines obtained from animals primed with peptide epitope recognize endogenously synthesized HIV antigen. The choice of transgenic mouse model to be used for such an analysis depends upon the epitope(s) that is being evaluated. In addition to HLA-A*0201/K^b transgenic mice, several other transgenic mouse models including mice with human A11, which may also be used to evaluate A3 epitopes, and B7 alleles have been characterized and others (e.g., transgenic mice for HLA-A1 and A24) are being developed. HLA-DR1 and HLA-DR3 mouse models have also been developed, which may be used to evaluate HTL epitopes.

EXAMPLE 5. ACTIVITY OF CTL-HTL CONJUGATED EPITOPES IN TRANSGENIC MICE

of a HIV CTL/HTL peptide conjugate whereby the vaccine composition comprises peptides administered to an HIV-infected patient or an individual at risk for HIV. The peptide composition can comprise multiple CTL and/or HTL epitopes. This analysis demonstrates enhanced immunogenicity that can be achieved by inclusion of one or more HTL epitopes in a vaccine composition. Such a peptide composition can comprise an HTL epitope conjugated to a preferred CTL epitope containing, for example, at least one CTL epitope, or an analog of that epitope. The peptides may be lipidated, if desired.

- [00391] Immunization procedures: Immunization of transgenic mice is performed as described (Alexander et al., J. Immunol. 159:4753-4761, 1997). For example, A2/K^b mice, which are transgenic for the human HLA A2.1 allele and are useful for the assessment of the immunogenicity of HLA-A*0201 motif- or HLA-A2 supermotif-bearing epitopes, are primed subcutaneously (base of the tail) with a 0.1 ml of peptide in Incomplete Freund's Adjuvant, or if the peptide composition is a lipidated CTL/HTL conjugate, in DMSO/saline or if the peptide composition is a polypeptide, in PBS or Incomplete Freund's Adjuvant. Seven days after priming, splenocytes obtained from these animals are restimulated with syngenic irradiated LPS-activated lymphoblasts coated with peptide.
- [00392] Cell lines: Target cells for peptide-specific cytotoxicity assays are Jurkat cells transfected with the HLA-A2.1/K^b chimeric gene (e.g., Vitiello et al., J. Exp. Med. 173:1007, 1991).
- [00393] In vitro CTL activation: One week after priming, spleen cells (30x10⁶ cells/flask) are co-cultured at 37°C with syngeneic, irradiated (3000 rads), peptide coated lymphoblasts (10x10⁶ cells/flask) in 10 ml of culture medium/T25 flask. After six days, effector cells are harvested and assayed for cytotoxic activity.
- Assay for cytotoxic activity: Target cells (1.0 to 1.5x10⁶) are incubated at 37°C in [00394] the presence of 200 µl of ⁵¹Cr. After 60 minutes, cells are washed three times and resuspended in R10 medium. Peptide is added where required at a concentration of 1 ug/ml. For the assay, 10^4 51Cr-labeled target cells are added to different concentrations of effector cells (final volume of 200 µl) in U-bottom 96-well plates. After a 6 hour incubation period at 37°C, a 0.1 ml aliquot of supernatant is removed from each well and radioactivity is determined in a Micromedic automatic gamma counter. The percent specific lysis is determined by the formula: percent specific release = 100 x (experimental release - spontaneous release)/(maximum release - spontaneous release). To facilitate comparison between separate CTL assays run under the same conditions, % 51Cr release data is expressed as lytic units/10⁶ cells. One lytic unit is arbitrarily defined as the number of effector cells required to achieve 30% lysis of 10,000 target cells in a 6 hour 51Cr release assay. To obtain specific lytic units/106, the lytic units/106 obtained in the absence of peptide is subtracted from the lytic units/10⁶ obtained in the presence of peptide. For example, if 30% ⁵¹Cr release is obtained at the effector (E): target (T) ratio of 50:1 (i.e., 5x10⁵ effector cells for 10,000 targets) in the absence of peptide and 5:1 (i.e., 5x10⁴

effector cells for 10,000 targets) in the presence of peptide, the specific lytic units would be: $[(1/50,000)-(1/500,000)] \times 10^6 = 18 \text{ LU}.$

[00395] The results are analyzed to assess the magnitude of the CTL responses of animals injected with the immunogenic CTL/HTL conjugate vaccine preparation and are compared to the magnitude of the CTL response achieved using the CTL epitope as outlined in above. Analyses similar to this may be performed to evaluate the immunogenicity of peptide conjugates containing multiple CTL epitopes and/or multiple HTL epitopes. In accordance with these procedures it is found that a CTL response is induced, and concomitantly that an HTL response is induced upon administration of such compositions.

EXAMPLE 6. SELECTION OF CTL AND HTL EPITOPES FOR INCLUSION IN AN HIV-SPECIFIC VACCINE.

- [00396] This example illustrates the procedure for the selection of peptide epitopes for vaccine compositions of the invention. The peptides in the composition can be in the form of a nucleic acid sequence, either single or one or more sequences (i.e., minigene) that encodes peptide(s), or can be single and/or polyepitopic peptides.
- [00397] The following principles are utilized when selecting an array of epitopes for inclusion in a vaccine composition. Each of the following principles is balanced in order to make the selection.
- [00398] Epitopes are selected which, upon administration, mimic immune responses that correlate with virus clearance. For example, if it has been observed that patients who clear HIV generate an immune response to at least 3 epitopes on at least one HIV antigen, then 3-4 epitopes should be included for HLA class I. A similar rationale is used to determine HLA class II epitopes.
- [00399] When selecting an array of HIV epitopes, it is preferred that at least some of the epitopes are derived from early and late proteins. The early proteins of HIV are expressed when the virus is replicating, either following acute or dormant infection. Therefore, it is particularly preferred to use epitopes from early stage proteins to alleviate disease manifestations at the earliest stage possible.
- [00400] Epitopes are often selected that have a binding affinity of an IC₅₀ of 500 nM or less for an HLA class I molecule, or for class II, an IC₅₀ of 1000 nM or less.

- [00401] Sufficient supermotif bearing peptides, or a sufficient array of allele-specific motif bearing peptides, are selected to give broad population coverage. For example, epitopes are selected to provide at least 80% population coverage. A Monte Carlo analysis, a statistical evaluation known in the art, can be employed to assess breadth, or redundancy, of population coverage.
- [00402] When creating a polyepitopic compositions, e.g. a minigene, it is typically desirable to generate the smallest peptide possible that encompasses the epitopes of interest. The principles employed are similar, if not the same, as those employed when selecting a peptide comprising nested epitopes.
- [00403] In cases where the sequences of multiple variants of the same target protein are available, potential peptide epitopes can also be selected on the basis of their conservancy. For example, a criterion for conservancy may define that the entire sequence of an HLA class I binding peptide or the entire 9-mer core of a class II binding peptide be conserved in a designated percentage of the sequences evaluated for a specific protein antigen.
- [00404] Peptide epitopes for inclusion in vaccine compositions are, for example, selected from those listed in Tables 6-9 or Figures 1A-4. A vaccine composition comprised of selected peptides, when administered, is safe, efficacious, and elicits an immune response similar in magnitude of an immune response that clears an acute HIV infection.

EXAMPLE 7. CONSTRUCTION OF MINIGENE MULTI-EPITOPE DNA PLASMIDS

- [00405] This example provides general guidance for the construction of a minigene expression plasmid. Minigene plasmids may, of course, contain various configurations of CTL and/or HTL epitopes or epitope analogs as described herein. Expression plasmids have been constructed and evaluated as described, for example, in co-pending U.S.S.N. 09/311,784 filed 5/13/99 and in Ishioka *et al.*, *J. Immunol.* 162:3915-3925, 1999. An example of such a plasmid for the expression of HIV epitopes is shown in Figure 2, which illustrates the orientation of HIV peptide epitopes in a minigene construct.
- [00406] A minigene expression plasmid typically includes multiple CTL and HTL peptide epitopes. In the present example, HLA-A2, -A3, -B7 supermotif-bearing peptide epitopes and HLA-A1 and -A24 motif-bearing peptide epitopes are used in conjunction with DR supermotif-bearing epitopes and/or DR3 epitopes (Figure 2). Preferred epitopes are

identified, for example, in Tables 6-9 and Figures 1A-4. HLA class I supermotif or motif-bearing peptide epitopes derived from multiple HIV antigens, are selected such that multiple supermotifs/motifs are represented to ensure broad population coverage. Similarly, HLA class II epitopes are selected from multiple HIV antigens to provide broad population coverage, *i.e.* both HLA DR-1-4-7 supermotif-bearing epitopes and HLA DR-3 motif-bearing epitopes are selected for inclusion in the minigene construct. The selected CTL and HTL epitopes are then incorporated into a minigene for expression in an expression vector.

- [00407] Such a construct may additionally include sequences that direct the HTL epitopes to the endoplasmic reticulum. For example, the Ii protein may be fused to one or more HTL epitopes as described in co-pending application U.S.S.N. 09/311,784 filed 5/13/99, wherein the CLIP sequence of the Ii protein is removed and replaced with an HLA class II epitope sequence os that HLA class II epitope is directed to the endoplasmic reticulum, where the epitope binds to an HLA class II molecules.
- [00408] This example illustrates the methods to be used for construction of a minigenebearing expression plasmid. Other expression vectors that may be used for minigene compositions are available and known to those of skill in the art.
- [00409] The minigene DNA plasmid contains a consensus Kozak sequence and a consensus murine kappa Ig-light chain signal sequence followed by CTL and/or HTL epitopes selected in accordance with principles disclosed herein. The construct can also include, for example, The sequence encodes an open reading frame fused to the Myc and His antibody epitope tag coded for by the pcDNA 3.1 Myc-His vector.
- [00410] Overlapping oligonucleotides, for example eight oligonucleotides, averaging approximately 70 nucleotides in length with 15 nucleotide overlaps, are synthesized and HPLC-purified. The oligonucleotides encode the selected peptide epitopes as well as appropriate linker nucleotides, Kozak sequence, and signal sequence. The final multiepitope minigene is assembled by extending the overlapping oligonucleotides in three sets of reactions using PCR. A Perkin/Elmer 9600 PCR machine is used and a total of 30 cycles are performed using the following conditions: 95°C for 15 sec, annealing temperature (5° below the lowest calculated Tm of each primer pair) for 30 sec, and 72°C for 1 min.
- [00411] For the first PCR reaction, 5 µg of each of two oligonucleotides are annealed and extended: Oligonucleotides 1+2, 3+4, 5+6, and 7+8 are combined in 100 µl reactions

containing *Pfu* polymerase buffer (1x= 10 mM KCL, 10 mM (NH₄)₂SO₄, 20 mM Trischloride, pH 8.75, 2 mM MgSO₄, 0.1% Triton X-100, 100 μg/ml BSA), 0.25 mM each dNTP, and 2.5 U of *Pfu* polymerase. The full-length dimer products are gel-purified, and two reactions containing the product of 1+2 and 3+4, and the product of 5+6 and 7+8 are mixed, annealed, and extended for 10 cycles. Half of the two reactions are then mixed, and 5 cycles of annealing and extension carried out before flanking primers are added to amplify the full length product for 25 additional cycles. The full-length product is gel-purified and cloned into pCR-blunt (Invitrogen) and individual clones are screened by sequencing.

EXAMPLE 8. THE PLASMID CONSTRUCT AND THE DEGREE TO WHICH IT INDUCES IMMUNOGENICITY.

- [00412] The degree to which a plasmid construct, for example a plasmid constructed in accordance as above is able to induce immunogenicity can be evaluated *in vitro* by testing for epitope presentation by APC following transduction or transfection of the APC with an epitope-expressing nucleic acid construct. Such a study determines "antigenicity" and allows the use of human APC. The assay determines the ability of the epitope to be presented by the APC in a context that is recognized by a T cell by quantifying the density of epitope-HLA class I complexes on the cell surface. Quantitation can be performed by directly measuring the amount of peptide eluted from the APC (see, e.g., Sijts et al., J. Immunol. 156:683-692, 1996; Demotz et al., Nature 342:682-684, 1989); or the number of peptide-HLA class I complexes can be estimated by measuring the amount of lysis or lymphokine release induced by infected or transfected target cells, and then determining the concentration of peptide necessary to obtained equivalent levels of lysis or lymphokine release (see, e.g., Kageyama et al., J. Immunol. 154:567-576, 1995).
- [00413] Atlernatively, immunogenicity can be evaluated through *in vivo* injections into mice and subsequent *in vitro* assessment of CTL and HTL activity, which are analysed using cytotoxicity and proliferation assays, respectively, as detailed *e.g.*, in copending U.S.S.N. 09/311,784 filed 5/13/99 and Alexander *et al.*, *Immunity* 1:751-761, 1994.
- [00414] For example, to assess the capacity of a DNA minigene construct (e.g., a pMin minigene construct generated as decribed in U.S.S.N. 09/311,784) containing at least one

HLA-A2 supermotif peptide to induce CTLs *in vivo*, HLA-A2.1/K^b transgenic mice, for example, are immunized intramuscularly with 100 µg of naked cDNA. As a means of comparing the level of CTLs induced by cDNA immunization, a control group of animals is also immunized with an actual peptide composition that comprises multiple epitopes synthesized as a single polypeptide as they would be encoded by the minigene.

[00415] Splenocytes from immunized animals are stimulated twice with each of the respective compositions (peptide epitopes encoded in the minigene or the polyepitopic peptide), then assayed for peptide-specific cytotoxic activity in a ⁵¹Cr release assay. The results indicate the magnitude of the CTL response directed against the A2-restricted epitope, thus indicating the *in vivo* immunogenicity of the minigene vaccine and polyepitopic vaccine. It is, therefore, found that the minigene elicits immune responses directed toward the HLA-A2 supermotif peptide epitopes as does the polyepitopic peptide vaccine. A similar analysis is also performed using other HLA-A3 and HLA-B7 transgenic mouse models to assess CTL induction by HLA-A3 and HLA-B7 motif or supermotif epitopes.

[00416] To assess the capacity of a class II epitope encoding minigene to induce HTLs *in vivo*, DR transgenic mice, or for those epitope that cross react with the appropriate mouse MHC molecule, I-A^b-restricted mice, for example, are immunized intramuscularly with 100 μg of plasmid DNA. As a means of comparing the level of HTLs induced by DNA immunization, a group of control animals is also immunized with an actual peptide composition emulsified in complete Freund's adjuvant. CD4+ T cells, *i.e.* HTLs, are purified from splenocytes of immunized animals and stimulated with each of the respective compositions (peptides encoded in the minigene). The HTL response is measured using a ³H-thymidine incorporation proliferation assay, (*see*, *e.g.*, Alexander et al. Immunity 1:751-761, 1994). The results indicate the magnitude of the HTL response, thus demonstrating the *in vivo* immunogenicity of the minigene.

DNA minigenes, constructed as described above or below, may also be evaluated as a vaccine in combination with a boosting agent using a prime boost protocol. The boosting agent can consist of recombinant protein (e.g., Barnett et al., Aids Res. and Human Retroviruses 14, Supplement 3:S299-S309, 1998) or recombinant vaccinia, for example, expressing a minigene or DNA encoding the complete protein of interest (see, e.g., Hanke et al., Vaccine 16:439-445, 1998; Sedegah et al., Proc. Natl. Acad. Sci USA

95:7648-53, 1998; Hanke and McMichael, *Immunol. Letters* 66:177-181, 1999; and Robinson *et al.*, *Nature Med.* 5:526-34, 1999).

[00418] For example, the efficacy of the DNA minigene used in a prime boost protocol is initially evaluated in transgenic mice. In this example, A2.1/K^b transgenic mice are immunized IM with 100 μg of a DNA minigene encoding the immunogenic peptides including at least one HLA-A2 supermotif-bearing peptide. After an incubation period (ranging from 3-9 weeks), the mice are boosted IP with 10⁷ pfu/mouse of a recombinant vaccinia virus expressing the same sequence encoded by the DNA minigene. Control mice are immunized with 100 μg of DNA or recombinant vaccinia without the minigene sequence, or with DNA encoding the minigene, but without the vaccinia boost. After an additional incubation period of two weeks, splenocytes from the mice are immediately assayed for peptide-specific activity in an ELISPOT assay. Additionally, splenocytes are stimulated *in vitro* with the A2-restricted peptide epitopes encoded in the minigene and recombinant vaccinia, then assayed for peptide-specific activity in an IFN-γ ELISA.

[00419] It is found that the minigene utilized in a prime-boost protocol elicits greater immune responses toward the HLA-A2 supermotif peptides than with DNA alone. Such an analysis can also be performed using HLA-A11 or HLA-B7 transgenic mouse models to assess CTL induction by HLA-A3 or HLA-B7 motif or supermotif epitopes.

[00420] The use of prime boost protocols in humans is described in below.

EXAMPLE 9. PEPTIDE COMPOSITION FOR PROPHYLACTIC USES

[00421] Vaccine compositions of the present invention can be used to prevent HIV infection in persons who are at risk for such infection. For example, a polyepitopic peptide epitope composition (or a nucleic acid comprising the same) containing multiple CTL and HTL epitopes, which are also selected to target greater than 80% of the population, is administered to individuals at risk for HIV infection.

[00422] For example, a peptide-based composition can be provided as a single polypeptide that encompasses multiple epitopes. The vaccine is typically administered in a physiological solution that comprises an adjuvant, such as Incomplete Freunds Adjuvant. The dose of peptide for the initial immunization is from about 1 to about 50,000 μg, generally 100-5,000 μg, for a 70 kg patient. The initial administration of vaccine is

followed by booster dosages at 4 weeks followed by evaluation of the magnitude of the immune response in the patient, by techniques that determine the presence of epitope-specific CTL populations in a PBMC sample. Additional booster doses are administered as required. The composition is found to be both safe and efficacious as a prophylaxis against HIV infection.

[00423] Alternatively, a composition typically comprising transfecting agents can be used for the administration of a nucleic acid-based vaccine in accordance with methodologies known in the art and disclosed herein.

EXAMPLE 10. POLYEPITOPIC VACCINE COMPOSITIONS DERIVED FROM NATIVE HIV SEQUENCES

[00424] A native HIV polyprotein sequence is screened, preferably using computer algorithms defined for each class I and/or class II supermotif or motif, to identify "relatively short" regions of the polyprotein that comprise multiple epitopes and is preferably less in length than an entire native antigen. This relatively short sequence that contains multiple distinct, even overlapping, epitopes is selected and used to generate a minigene construct. The construct is engineered to express the peptide, which corresponds to the native protein sequence. The "relatively short" peptide is generally less than 250 amino acids in length, often less than 100 amino acids in length, preferably less than 75 amino acids in length, and more preferably less than 50 amino acids in length. The protein sequence of the vaccine composition is selected because it has maximal number of epitopes contained within the sequence, *i.e.*, it has a high concentration of epitopes. As noted herein, epitope motifs may be nested or overlapping, for example, two 9-mer epitopes and one 10-mer epitope can be present in a 10 amino acid peptide. Such a vaccine composition is administered for therapeutic or prophylactic purposes.

[00425] The vaccine composition will preferably include, for example, three CTL epitopes and at least one HTL epitope from HIV. This polyepitopic native sequence is administered either as a peptide or as a nucleic acid sequence which encodes the peptide. Alternatively, an analog can be made of this native sequence, whereby one or more of the epitopes comprise substitutions that alter the cross-reactivity and/or binding affinity properties of the polyepitopic peptide.

- [00426] The embodiment of this example provides for the possibility that an as yet undiscovered aspect of immune system processing will apply to the native nested sequence and thereby facilitate the production of therapeutic or prophylactic immune response-inducing vaccine compositions. Additionally such an embodiment provides for the possibility of motif-bearing epitopes for an HLA makeup that is presently unknown. Furthermore, this embodiment (absent analogs) directs the immune response to multiple peptide sequences that are actually present in native HIV antigens thus avoiding the need to evaluate any junctional epitopes. Lastly, the embodiment provides an economy of scale when producing nucleic acid vaccine compositions.
- [00427] Related to this embodiment, computer programs can be derived in accordance with principles in the art, which identify in a target sequence, the greatest number of epitopes per sequence length.

EXAMPLE 11. POLYEPITOPIC VACCINE COMPOSITIONS DIRECTED TO MULTIPLE DISEASES

- [00428] The HIV peptide epitopes of the present invention are used in conjunction with peptide epitopes from target antigens related to one or more other diseases, to create a vaccine composition that is useful for the prevention or treatment of HIV as well as the one or more other disease(s). Examples of the other diseases include, but are not limited to, HCV and HBV.
- [00429] For example, a polyepitopic peptide composition comprising multiple CTL and HTL epitopes that target greater than 98% of the population may be created for administration to individuals at risk for both HBV and HIV infection. The composition can be provided as a single polypeptide that incorporates the multiple epitopes from the various disease-associated sources, or can be administered as a composition comprising one or more discrete epitopes.

EXAMPLE 12. USE OF PEPTIDES TO EVALUATE AN IMMUNE RESPONSE

[00430] Peptides of the invention may be used to analyze an immune response for the presence of specific CTL or HTL populations directed to HIV. Such an analysis may be

performed in a manner as that described by Ogg et al., Science 279:2103-2106, 1998. In the following example, peptides in accordance with the invention are used as a reagent for diagnostic or prognostic purposes, not as an immunogen.

In this example highly sensitive human leukocyte antigen tetrameric complexes [00431] ("tetramers") are used for a cross-sectional analysis of, for example, HIV HLA-A*0201specific CTL frequencies from HLA A*0201-positive individuals at different stages of infection or following immunization using an HIV peptide containing an A*0201 motif. Tetrameric complexes are synthesized as described (Musey et al., N. Engl. J. Med. 337:1267, 1997). Briefly, purified HLA heavy chain (A*0201 in this example) and β2microglobulin are synthesized by means of a prokaryotic expression system. The heavy chain is modified by deletion of the transmembrane-cytosolic tail and COOH-terminal addition of a sequence containing a BirA enzymatic biotinylation site. The heavy chain, β2-microglobulin, and peptide are refolded by dilution. The 45-kD refolded product is isolated by fast protein liquid chromatography and then biotinylated by BirA in the presence of biotin (Sigma, St. Louis, Missouri), adenosine 5'triphosphate and magnesium. Streptavidin-phycoerythrin conjugate is added in a 1:4 molar ratio, and the tetrameric product is concentrated to 1 mg/ml. The resulting product is referred to as tetramerphycoerythrin.

[00432] For the analysis of patient blood samples, approximately one million PBMCs are centrifuged at 300 x g for 5 minutes and resuspended in 50 µl of cold phosphate-buffered saline. Tri-color analysis is performed with the tetramer-phycoerythrin, along with anti-CD8-Tricolor, and anti-CD38. The PBMCs are incubated with tetramer and antibodies on ice for 30 to 60 min and then washed twice before formaldehyde fixation. Gates are applied to contain >99.98% of control samples. Controls for the tetramers include both A*0201-negative individuals and A*0201-positive uninfected donors. The percentage of cells stained with the tetramer is then determined by flow cytometry. The results indicate the number of cells in the PBMC sample that contain epitope-restricted CTLs, thereby readily indicating the extent of immune response to the HIV epitope, and thus the stage of infection with HIV, the status of exposure to HIV, or exposure to a vaccine that elicits a protective or therapeutic response.

EXAMPLE 13. USE OF PEPTIDE EPITOPES TO EVALUATE RECALL RESPONSES

- [00433] The peptide epitopes of the invention are used as reagents to evaluate T cell responses, such as acute or recall responses, in patients. Such an analysis may be performed on patients who have recovered from infection, who are chronically infected with HIV, or who have been vaccinated with an HIV vaccine.
- [00434] For example, the class I restricted CTL response of persons who have been vaccinated may be analyzed. The vaccine may be any HIV vaccine. PBMC are collected from vaccinated individuals and HLA typed. Appropriate peptide epitopes of the invention that, optimally, bear supermotifs to provide cross-reactivity with multiple HLA supertype family members, are then used for analysis of samples derived from individuals who bear that HLA type.
- [00435] PBMC from vaccinated individuals are separated on Ficoll-Histopaque density gradients (Sigma Chemical Co., St. Louis, MO), washed three times in HBSS (GIBCO Laboratories), resuspended in RPMI-1640 (GIBCO Laboratories) supplemented with L-glutamine (2mM), penicillin (50U/ml), streptomycin (50 μg/ml), and Hepes (10mM) containing 10% heat-inactivated human AB serum (complete RPMI) and plated using microculture formats. A synthetic peptide comprising an epitope of the invention is added at 10 μg/ml to each well and HBV core 128-140 epitope is added at 1 μg/ml to each well as a source of T cell help during the first week of stimulation.
- [00436] In the microculture format, 4 x 10⁵ PBMC are stimulated with peptide in 8 replicate cultures in 96-well round bottom plate in 100 μl/well of complete RPMI. On days 3 and 10, 100 ml of complete RPMI and 20 U/ml final concentration of rIL-2 are added to each well. On day 7 the cultures are transferred into a 96-well flat-bottom plate and restimulated with peptide, rIL-2 and 10⁵ irradiated (3,000 rad) autologous feeder cells. The cultures are tested for cytotoxic activity on day 14. A positive CTL response requires two or more of the eight replicate cultures to display greater than 10% specific ⁵¹Cr release, based on comparison with uninfected control subjects as previously described (Rehermann, *et al.*, *Nature Med.* 2:1104,1108, 1996; Rehermann *et al.*, *J. Clin. Invest.* 97:1655-1665, 1996; and Rehermann *et al. J. Clin. Invest.* 98:1432-1440, 1996).
- [00437] Target cell lines are autologous and allogeneic EBV-transformed B-LCL that are either purchased from the American Society for Histocompatibility and Immunogenetics

(ASHI, Boston, MA) or established from the pool of patients as described (Guilhot, et al. J. Virol. 66:2670-2678, 1992).

- [00438] Cytotoxicity assays are performed in the following manner. Target cells consist of either allogeneic HLA-matched or autologous EBV-transformed B lymphoblastoid cell line that are incubated overnight with the synthetic peptide epitope of the invention at 10 μM, and labeled with 100 μCi of ⁵¹Cr (Amersham Corp., Arlington Heights, IL) for 1 hour after which they are washed four times with HBSS.
- [00439] Cytolytic activity is determined in a standard 4-h, split well ⁵¹Cr release assay using U-bottomed 96 well plates containing 3,000 targets/well. Stimulated PBMC are tested at effector/target (E/T) ratios of 20-50:1 on day 14. Percent cytotoxicity is determined from the formula: 100 x [(experimental release-spontaneous release)/maximum release-spontaneous release)]. Maximum release is determined by lysis of targets by detergent (2% Triton X-100; Sigma Chemical Co., St. Louis, MO). Spontaneous release is <25% of maximum release for all experiments.
- [00440] The results of such an analysis indicate the extent to which HLA-restricted CTL populations have been stimulated by previous exposure to HIV or an HIV vaccine.
- The class II restricted HTL responses may also be analyzed. Purified PBMC are cultured in a 96-well flat bottom plate at a density of 1.5x10⁵ cells/well and are stimulated with 10 μg/ml synthetic peptide, whole antigen, or PHA. Cells are routinely plated in replicates of 4-6 wells for each condition. After seven days of culture, the medium is removed and replaced with fresh medium containing 10U/ml IL-2. Two days later, 1 μCi ³H-thymidine is added to each well and incubation is continued for an additional 18 hours. Cellular DNA is then harvested on glass fiber mats and analyzed for ³H-thymidine incorporation. Antigen-specific T cell proliferation is calculated as the ratio of ³H-thymidine incorporation in the presence of antigen divided by the ³H-thymidine incorporation in the absence of antigen.

EXAMPLE 14. INDUCTION OF SPECIFIC CTL RESPONSE IN HUMANS

[00442] A human clinical trial for an immunogenic composition comprising CTL and HTL epitopes of the invention is set up as an IND Phase I, dose escalation study and carried out

as a randomized, double-blind, placebo-controlled trial. Such a trial is designed, for example, as follows:

[00443] A total of about 27 subjects are enrolled and divided into 3 groups:

Group I: 3 subjects are injected with placebo and 6 subjects are injected with 5 µg of peptide composition;

Group II: 3 subjects are injected with placebo and 6 subjects are injected with 50 µg peptide composition;

Group III: 3 subjects are injected with placebo and 6 subjects are injected with 500 µg of peptide composition.

- [00444] After 4 weeks following the first injection, all subjects receive a booster inoculation at the same dosage.
- [00445] The endpoints measured in this study relate to the safety and tolerability of the peptide composition as well as its immunogenicity. Cellular immune responses to the peptide composition are an index of the intrinsic activity of this the peptide composition, and can therefore be viewed as a measure of biological efficacy. The following summarize the clinical and laboratory data that relate to safety and efficacy endpoints.
- [00446] Safety: The incidence of adverse events is monitored in the placebo and drug treatment group and assessed in terms of degree and reversibility.
- [00447] Evaluation of Vaccine Efficacy: For evaluation of vaccine efficacy, subjects are bled before and after injection. Peripheral blood mononuclear cells are isolated from fresh heparinized blood by Ficoll-Hypaque density gradient centrifugation, aliquoted in freezing media and stored frozen. Samples are assayed for CTL and HTL activity.
- [00448] The vaccine is found to be both safe and efficacious.

EXAMPLE 15. PHASE II TRIALS IN PATIENTS INFECTED WITH HIV

[00449] Phase II trials are performed to study the effect of administering the CTL-HTL peptide compositions to HIV-infected patients. The main objectives of the trials are to determine an effective dose and regimen for inducing CTLs in chronically infected HIV patients, to establish the safety of inducing a CTL and HTL response in these patients, and to see to what extent activation of CTLs improves the clinical picture of chronically infected HIV patients, as manifested by a reduction in viral load and an increase in CD4⁺ cells counts. Such a study is designed, for example, as follows:

- [00450] The studies are performed in multiple centers. The trial design is an open-label, uncontrolled, dose escalation protocol wherein the peptide composition is administered as a single dose followed six weeks later by a single booster shot of the same dose. The dosages are 50, 500 and 5,000 micrograms per injection. Drug-associated adverse effects (severity and reversibility) are recorded.
- [00451] There are three patient groupings. The first group is injected with 50 micrograms of the peptide composition and the second and third groups with 500 and 5,000 micrograms of peptide composition, respectively. The patients within each group range in age from 21-65, include both males and females, and represent diverse ethnic backgrounds. All of them are infected with HIV for over five years and are HCV, HBV and delta hepatitis virus (HDV) negative, but have positive levels of HIV antigen.
- [00452] The viral load and CD4⁺ levels are monitored to assess the effects of administering the peptide compositions. The vaccine composition is found to be both safe and efficacious in the treatment of HIV infection.

EXAMPLE 16. INDUCTION OF CTL RESPONSES USING A PRIME BOOST PROTOCOL

- [00453] A prime boost protocol can also be used for the administration of the vaccine to humans. Such a vaccine regimen can include an initial administration of, for example, naked DNA followed by a boost using recombinant virus encoding the vaccine, or recombinant protein/polypeptide or a peptide mixture administered in an adjuvant.
- [00454] For example, the initial immunization is performed using an expression vector, such as that constructed above, in the form of naked nucleic acid administered IM (or SC or ID) in the amounts of 0.5-5 mg at multiple sites. The nucleic acid (0.1 to 1000 μg) can also be administered using a gene gun. Following an incubation period of 3-4 weeks, a booster dose is then administered. The booster is, for example, recombinant fowlpox virus administered at a dose of 5-10⁷ to 5x10⁹ pfu. An alternative recombinant virus, such as an MVA, canarypox, adenovirus, or adeno-associated virus, can also be used for the booster, or the polyepitopic protein or a mixture of the peptides can be administered. For evaluation of vaccine efficacy, patient blood samples are obtained before immunization as well as at intervals following administration of the initial vaccine and booster doses of the

vaccine. Peripheral blood mononuclear cells are isolated from fresh heparinized blood by Ficoll-Hypaque density gradient centrifugation, aliquoted in freezing media and stored frozen. Samples are assayed for CTL and HTL activity.

[00455] Analysis of the results indicates that a magnitude of sufficient response to achieve protective immunity against HIV is generated.

EXAMPLE 17. ADMINISTRATION OF VACCINE COMPOSITIONS USING DENDRITIC CELLS

- [00456] Vaccines comprising peptide epitopes of the invention can be administered using APCs, or "professional" APCs such as DC. In this example, the peptide-pulsed DC are administered to a patient to stimulate a CTL response *in vivo*. In this method, dendritic cells are isolated, expanded, and pulsed with a vaccine comprising peptide CTL and HTL epitopes of the invention. The dendritic cells are infused back into the patient to elicit CTL and HTL responses *in vivo*. The induced CTL and HTL then destroy or facilitate destruction of the specific target cells that bear the proteins from which the epitopes in the vaccine are derived.
- [00457] For example, a cocktail of epitope-bearing peptides is administered *ex vivo* to PBMC, or isolated DC therefrom. A pharmaceutical to facilitate harvesting of DC can be used, such as ProgenipoietinTM (Monsanto, St. Louis, MO) or GM-CSF/IL-4. After pulsing the DC with peptides and prior to reinfusion into patients, the DC are washed to remove unbound peptides.
- [00458] As appreciated clinically, and readily determined by one of skill based on clinical outcomes, the number of DC reinfused into the patient can vary (see, e.g., Nature Med. 4:328, 1998; Nature Med. 2:52, 1996 and Prostate 32:272, 1997). Although 2-50 x 10⁶ DC per patient are typically administered, larger number of DC, such as 10⁷ or 10⁸ can also be provided. Such cell populations typically contain between 50-90% DC.
- [00459] In some embodiments, peptide-loaded PBMC are injected into patients without purification of the DC. For example, PBMC containing DC generated after treatment with an agent such as Progenipoietin™ are injected into patients without purification of the DC. The total number of PBMC that are administered often ranges from 10⁸ to 10¹⁰. Generally, the cell doses injected into patients is based on the percentage of DC in the

blood of each patient, as determined, for example, by immunofluorescence analysis with specific anti-DC antibodies. Thus, for example, if ProgenipoietinTM mobilizes 2% DC in the peripheral blood of a given patient, and that patient is to receive 5 x 10^6 DC, then the patient will be injected with a total of 2.5×10^8 peptide-loaded PBMC. The percent DC mobilized by an agent such as ProgenipoietinTM is typically estimated to be between 2-10%, but can vary as appreciated by one of skill in the art.

Ex vivo activation of CTL/HTL responses

[00460] Alternatively, ex vivo CTL or HTL responses to HIV antigens can be induced by incubating in tissue culture the patient's, or genetically compatible, CTL or HTL precursor cells together with a source of APC, such as DC, and the appropriate immunogenic peptides. After an appropriate incubation time (typically about 7-28 days), in which the precursor cells are activated and expanded into effector cells, the cells are infused back into the patient, where they will destroy or facilitate destruction of their specific target cells.

[00461] It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. All publications, patents, patent applications and sequence listings cited herein are hereby incorporated by reference in their entirety for all purposes.

TABLE 1

SUPERMOTIFS	POSITION	POSITION	POSITION
	2 (Primary	3 (Primary	C Terminus (Primary
	Anchor)	Anchor)	Anchor)
A1	T, I, <i>L, V, M, S</i>		F, W, Y
A2	L, I, V, M, A, T,		I, V, M, A, T, L
A3	V, S, M, A, T, L,		R,K
A24	Y, F, W, I, V, L, M, T		F, I, Y, W, L, M
·B7	P		V, I, L, F, M, W, Y, A
B27	R, H, K		F, Y, L, W, M, I, V, A
.B44	\mathbf{E}, D	_	F, W, L, I, M, V, A
B58	A, T, S		$\mathbf{F}, \mathbf{W}, \mathbf{Y}, L, I, V, M, A$
B62	Q, L, <i>I, V, M, P</i>		F, W, Y, <i>M, I, V, L, A</i>
MOTIFS		-	
Al	T, S, M		Y
Al		D , E , <i>A</i> , <i>S</i>	Y
A2.1	L, M, V, Q, I, A,		V, L, I, M, A, T
A3	L, M, V, I, S, A, T, F, C, G, D		K, Y, R, H, F, A
A11	V, T, M, L, I, S, A, G, N, C, D, F		K , <i>R</i> , <i>Y</i> , <i>H</i>
A24	Y, F, W, M		F, L, I, W
A*3101	M, V, T, A, L, I, S		R , <i>K</i>
A*3301	M, V, A, L, F, I, S, T		R, K
A*6801	A, V, T, <i>M, S, L, I</i>		R, K
B*0702	P		L, M, F, W, Y, A, I, V
B*3501	P		L, M, F, W, Y, I, V, A
B51	P		L, I, V, F, W, Y, A, M
B*5301	P		I, M, F, W, Y, A, L, V
B*5401	P		A, T, I, V, L, M, F, W,

Bolded residues are preferred, italicized residues are tolerated: A peptide is considered motif-bearing if it has primary anchors at each primary anchor position for a motif or supermotif as specified in the above table.

TABLE 2

SUPERMOTIFS	POSITION	POSITION	POSITION
	2 (Primary	3 (Primary	C Terminus (Primary
	Anchor)	Anchor)	Anchor)
Al	T, I, <i>L, V, M, S</i>		F, W, Y
A2	V, Q, A, T		I, V, L, M, A, T
A3	V, S, M, A, T, L,		R, K
A24	Y, F, W, I, V, L, M, T		F, I, Y, W, L, M
B7	P		V, I, L, F, M, W, Y, A
B27	R, H, K		F, Y, L, W, M, I, V, A
B58	A, T, S		F, W, Y, L, I, V, M, A
B62	Q, L, <i>I, V, M, P</i>		F, W, Y, M, I, V, L, A
MOTIFS			
A1	T, S, M		Y
A1		$\mathbf{D}, \mathbf{E}, A, S$	Y
A2.1	V, Q, A, T*		$\mathbf{V}, L, I, M, A, T$
A3.2	L, M, V, I, S, A,		K, Y, R, H, F, A
	T, F , <i>C</i> , <i>G</i> , <i>D</i>		
A11	V, T, M, L, I, S,		K , <i>R</i> , <i>H</i> , <i>Y</i>
	A, G, N, <i>C, D, F</i>		
A24	Y ,F, W		F, L, I, W

^{*}If 2 is V, or Q, the C-term is not L

Bolded residues are preferred, italicized residues are tolerated: A peptide is considered motif-bearing if it has primary anchors at each primary anchor position for a motif or supermotif as specified in the above table.

Table 4

HLA-supertype A1 A2 A3 A24 B7 B27 B44 B58	Verified ^a 501, A*2601, A*2602, A*702, A*0203, A*0203, A*0204, A*6 A*0214, A*6802, A*6901 101, A*3101, A*3301, A*301, A*301, A*3101, A*3402, A*3001 301, A*2402, A*3001 703, B*0704, B*0705, B*1 503, B*3504, B*3505, B*2 502, B*5601, B*5602, B*6 801 402, B*1509, B*2702, B*2 801, B*3901, B*3902, B*7 801, B*3901, B*3902, B*7 802, B*3701, B*4402, B*4 B*4002, B*4006	Predicted ^b 3201 A*0102, A*2604, A*3601, A*4301, A*8001 A*0208, A*0210, A*0211, A*0212, A*0213 5801 A*0302, A*1102, A*2603, A*3302, A*3401, A*3402, A*6601, A*6602, A*7401 A*2403, A*2403, A*2404, A*3002, A*3003 B*1511, B*4201, B*5901 7701, B*2701, B*2707, B*2708, B*3802, B*3903, B*3904, B*3905, B*4801, B*4801, B*1510, B*1513, B*1503 B*4101, B*4501, B*4701, B*501 B*3905, B*4801, B*4801, B*4501, B*5001
B62	B*1501, B*1502, B*1513, B*5201	B*1301, B*1302, B*1504, B*1505, B*1506, B*1507, B*1515 B*1510 B*1521 B*1512 B*1514 B*1510

- Verified alleles include alleles whose specificity has been determined by pool sequencing analysis, peptide binding assays, or by analysis of the sequences of CTL epitopes.
- Predicted alleles are alleles whose specificity is predicted on the basis of B and F pocket structure to overlap with the supertype specificity.

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Table 5. Compiled rankings and similarity assignments.

	1.0	3.3	4.0	4.5	5.5	8.2	6.7	10.5	11.0	11.3	11.8	12.2	12.2	113.2	113.7	114.2	16.55	153	168	182
Г	r	Ι	Μ	ഥ	>	X	H	Ø	W	H	Α	X	<u>a</u>	<u>æ</u>	<u>)</u>	<u>166</u> ,	H.	\$	9	<u>(1)</u>
K	1.0	2.7	0.9	8.9	7,2	7.5	8.5	9.2	10.5	11.3	11.5	12.2	12.7	12.8	13.7	9143	114.3	1143	1125	17.3
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	1.0	2.5	4.5	5.2	5.2	8.8	10.3	11.3	11.5	11.7	12.0	12.0	12.2	13.0	13,2	11440	1143	1143	[25]I	10.20
ı	Ι	ר	M	щ	>	X	H	H	Α	٠,	X	Ъ	0	~	(S)	(<u>Su</u>)	77	M	0	9
Н	1.0	2.0	5.8	6.2	8.2	8.7	- 0.6	.9.2	10.5	10.5	11.0	11.2	12.2	113.3	113.7	49.8	133	1153	(2)	~ []#
	Н	0	ш	Z	R	¥	<u>-</u>	D	S	L	7	M	Δ	Î.	(comp.	8	9	(84)	3	. W
	1.0	2.8	4.2	4.7	6.3	7.0	7.3	8.3	6.3	8.6	11.5	120	(3.5)	গান্ত্যন্ত	143	11525	(6,3)	(10)	(F.3)	118,22
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E	1.0	3.3	4.2	4.7	5.3	8.3	8.7	0.6	10.5	10.5	11.0	12.0	12.2	12.3	150	330	153	25(3))	82	(SXQ)
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	1.0	3.5	4.0	6.2	7.2	7.7	7.8	8.8	9.2	9.3	9.5	11.5	12.0	(B) 3	(F)	158	(()*(4))	16.7	0789	(8.3)
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	1.0	5.5	6.5	6.7	7.3	8.0	0.6	10.2	10.7	11.0	11.0	11.0	11.3	12.0	25%	3.9	L'ot	.50	6,00	(0.Z)
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Non-conserved (13.1-20) Semi-conserved (7.1-13) Conserved (1-7)

Table 5 (continued)

	1.0	6.2	6.3	7.3	8.0	6.7	10.0	10.3	10.7	11.0	11.5	11.7	11.7	12.0	12.2	12.7	13.0	14.2	1979	(6.0)
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	1.0	5.3	5.5	5.5	7.8	8.2	8.5	10.0	10.7	11.0	11.0	11.3	12.3	12.7	113.2	08390	1141,83	160	2°911	(65.3)
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H	1.0	4.7	5.0	5.7	6.5	7.8	8.3	8.8 8.9	10.5	10.5	10.5	12.2	12.2	12.3	13.7	(14.3)	(E)	16.3	SOF	ELI
	T	Д	S	A	Z	Δ	ш l	ග ී	Η	Ø	Λ	ψ.	4	Σ	()	3		ON THE PROPERTY OF THE PROPERT	7	
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s	1.0	4.0	4.2	4.7	5.3				l.			Alex		(18,3)	[H.5]	. 14.8		390		16.3
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	 	×	五	O	王 、	4	2		H	S	S	T	7	ď	,	<i>S</i> 20	310	~ C4C.	9))
	1.0	3.2	3.3	0.9	7.0	7.2	8.3	8.5	10.5	.8.	1.3	2.3	3.0	J.B	388	4.2	500	£ 19	133	(B)
Ø	7	3	Н 3	9 Z	X 7	D + 7	8 8	Р 8	7	T 10	V 1	S 1.	A 13	C 13	II.	7ê j	<u> </u>	M I		\$ &
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	1.0	3.5	0.9	6.3	7.2	7.2	7.8	9.2	9.5	10.2 💒	11.2	11.8	12.2	13,2	13.5	8	(0'%)[16.3	(6,3)	37.8
4	<u>ا</u>	Н	S	٠ ٧	H	O	Z	Ω	ш	C C	V	C C	M	€ ¥	×	*	. v		(H)	64.
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	1.0	3.2	4.5	5.8	8.9	7.2	2.7	8.5	8.7	10.5	10.7	11.8	12.8	1 5 3	%	12	(A) TO	10,3		(S.3)
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×	1.0	3.8	5.0	5.2	7.0	9.7	10.3	10.5	10.8	11.0	11.2	11.3	11.8	12.7	13.0	1.36.2				(C) (S)
	Σ	ļ	_	>	н	×	Ø	R	Y	H	٧	L	Ъ	×	ပ	غِد				2.5

Conserved (1-7)

Non-conserved (13.1-20)

Table 6. Recognition of variant peptides by CTL generated after one and five stimulations with the parent peptide.

	Binding	1 Stimulation	5 Stimulations
Peptide Sequence	IC50 (nM)	(SU)	(SU)
VLAEAMSQV	49.9	31.6	222.0
VLAEAMSQ A	23.8	17.0	133.5
VLAEAMSQI	70.9	21.2	246.1
VLAEAMS K V	230.5	10.8	130.9
VLAEAMS KA	69.4	NT	36.6
ILAEAMSQ A	29.3	4.0	49.7
ILAEAMS KA	72.4		
VLAEAMAAA	17	16.3	90.3

B. Env	134	(KL	.TPL	.CV	TL)
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B. EIIV 134 (NLIPLO	V I L)		
KLTPLCVTL	77.0	278.4	683.6
KITPLCVTL	461	231.8	700.8
Q LTPLCVTL	63.6	166.2	361.5
QI TPLCVTL	975	105.0	166.9
ELTPLCVTL	7190	91.7	100.0
KLTPFCVTL	87.3	36.1	75.4
KLTPLCVIL	356	77.2	29.1
KLTPLCV P L	14.6	9.6	14.8

Table 7. Conservation of EP HIV-1090 epitopes across clades, calculated as identity or immunological conservation

			<u>Total</u>	<u>C</u>	lade B	<u>C</u>	<u>lade C</u>
Protein	Sequence	Identity	Imm. Cons.	Identity	Imm. Cons.	Identity	Imm. Cons.
Pol 498	ILKEPVHGV	62%	87%	77%	86%	74%	95%
Gag 386	VLAEAMSQV	32%	93%	68%	91%	5%	94%
Pol 448	KLVGKLNWA	95%	96%	95%	95%	95%	98%
Env 134	KLTPLCVTL	80%	93%	90%	95%	89%	98%
Vpr 62	RILQQLLFI	51%	93%	68%	91%	61%	95%
Nef 221	LTFGWCFKL	49%	74%	77%	91%	47%	81%
Gag 271	MTNNPPIPV	20%	25%	91%	95%	8%	19%
Env 47	VTVYYGVPVWK	59%	87%	95%	100%	61%	92%
Pol 929	QMAVFIHNFK	84%	98%	100%	100%	94%	97%
Pol 98	VTIKIGGQLK	11%	71%	59%	91%	2%	89%
Pol 971	KIQNFRVYYR	80%	86%	91%	95%	79%	89%
Pol 347	AIFQSSMTK	53%	75%	77%	82%	44%	79%
Pol 722	KVYLAWVPAHK	14%	97%	82%	95%	3%	97%
Env 61	TTLFCASDAK	72%	89%	90%	100%	69%	92%
Nef 94	FPVRPQVPL	81%	93%	77%	95%	82%	94%
Gag 545	YPLASLRSLF	7%	29%	45%	95%	0%	0%
Rev 75	VPLQLPPL	44%	78%	68%	77%	27%	79%
Env 259	IPIHYCAPA	74%	95%	45%	95%	79%	97%
Gag 237	HPVHAGPIA	27%	54%	68%	95%	44%	94%
Pol 893	IPYNPQSQGVV	92%	96%	82%	95%	240%	97%
Env 250	CPKVSFEPI	45%	91%	77%	100%	45%	97%
	Mean	54%	81%	77%	93%	59%	84%
	n=	167		22		62	

		r			1		1		
					eque: trib		1		
						type			
Protein	Sequence	Conserved Epitopes*	SEQ ID NO	All	A	В	С	D	G
Pol 498	ILKEPVHGV	ILKEPVHGV	69	104	1	17	46	2	2
	, , , , , , , , , , , , , , , , , , , ,	ILREPVHGV	91	12			5		1
		ILKEPVHGA	92	10			2	1	
		ILKDPVHGV	93	8	5				
		KLKEPVHGV	94	3					
		ILKDPVHGA	95	2	2				
		ILKNPVHGV	96	2					
Gag 386	VLAEAMSQV	VLAEAMSQA	16	67	2	1	36	3	3
		VLAEAMSQV	10	54	7	15	3	1	
		VLAEAMSQT	99	11			9		
		VLAEAMSHA	100	6			4		
		ILAEAMSQV	101	5		3			
		ILAEAMSQA	58	3			2		
		VLAEAMSHV	103	2					
Pol 448	KLVGKLNWA	KLVGKLNWA	72	158	9	21	59	3	3
		KLIGKLNWA	105	1		<u></u>			
Env 134	KLTPLCVTL	KLTPLCVTL	9	134	8	19	55		
		QLTPLCVTL	19	5	2	1			
		KLTPLCVAL	108	3					
		RLTPLCVTL	109	3			3		
		KITPLCVTL	18	2		_			
Vpr 62	RILQQLLFI	RILQQLLFI	11	86	1	15	28	4	3
		RILQQLLFV	112	21	2		2		
		RTLQQLLFI	113	10		2	4		ļ
		RTLQQLLFV	114	10			1		<u>L</u> _
		RILQQLLFT	115	6		<u> </u>	2		<u> </u>
		RMLQQLLFI	116	4		1	3		L
		RVLQQLLFI	117	3			3		<u> -</u>
Nef 221	LTFGWCFKL	LTFGWCFKL	74	82	8	17	29		3
		LTFGWCYKL	119	31	1	2	17		1
I									

Env 47 V	MTNNPPIPV TVYYGVPVWK	MTSNPPIPV MTNNPPIPV MTSNPPVPV MTGNPPIPV MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK VTVYYGVPVWK	26 25 123 124 125 126 127 13 129	60 33 26 15 9 6 3	3 1 5 6	20	24 5 15 1 5 6 2	4	1
Env 47 V	TVYYGVPVWK	MTNNPPIPV MTSNPPVPV MTGNPPIPV MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK	25 123 124 125 126 127	33 26 15 9 6 3	1 5		5 15 1 5 6 2		
Env 47 V	TVYYGVPVWK	MTNNPPIPV MTSNPPVPV MTGNPPIPV MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK	25 123 124 125 126 127	33 26 15 9 6 3	1 5		5 15 1 5 6 2		
Env 47 V	TVYYGVPVWK	MTNNPPIPV MTSNPPVPV MTGNPPIPV MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK	25 123 124 125 126 127	33 26 15 9 6 3	1 5		5 15 1 5 6 2		
Env 47 V	TVYYGVPVWK	MTNNPPIPV MTSNPPVPV MTGNPPIPV MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK	25 123 124 125 126 127	33 26 15 9 6 3	1 5		5 15 1 5 6 2		
Env 47 V	TVYYGVPVWK	MTNNPPIPV MTSNPPVPV MTGNPPIPV MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK	25 123 124 125 126 127	33 26 15 9 6 3	1 5		5 15 1 5 6 2		
		MTSNPPVPV MTGNPPIPV MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK	123 124 125 126 127	26 15 9 6 3	5		15 1 5 6 2		1
		MTSNPPVPV MTGNPPIPV MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK	123 124 125 126 127	15 9 6 3	5	21	1 5 6 2		1
		MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK VTVYYGVPVWR	125 126 127	9 6 3		21	5 6 2		
		MTGNPPVPV MTNNPPVPV MTANPPVPV VTVYYGVPVWK VTVYYGVPVWR	126 127 13	6 3	6	21	6 2		
		MTNNPPVPV MTANPPVPV VTVYYGVPVWK VTVYYGVPVWR	126 127 13	3	6	21	2		
		MTANPPVPV VTVYYGVPVWK VTVYYGVPVWR	127 13		6	21			
		VTVYYGVPVWK VTVYYGVPVWR	13		6	21			
		VTVYYGVPVWR		99	6	21			
		VTVYYGVPVWR			"		30	3	1
Pol 929	OMANIETINE		120		i l			·	
Pol 929 0	OMANDELLIND		エムラ	40	1		18		<u> </u>
Dol 929 C	OMATIC TUNEDU		130	2				_	
Pol 929 C	ON A TENTE								
・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・	QMAVFIHNFK	QMAVFIHNFK	77	153	10	22	58	4	3
				ľ					
		QMAVFVHNFK	132	3			1		
		QMAVFVHNYK	133	2					
Pol 98 \	VTIKIGGQLK	VSIKVGGQIK	12	30			30		
		VTIKIGGQLK	<u>78</u>	18		13	1		
		VTVKIGGQLK	<u>136</u>	11	1	1		1	
		VTVRIGGQLK	137	6	3				
		VSIKVGGQIR	<u>138</u>	6			6		
		VSIRVGGQIK	<u>139</u>	4			4		
		VTIRIGGQLK	140	3		2			
		VTVKIGGQLR	141	3	1				
,		VTVKVGGQLK	<u>142</u>	3	ļl				
Pol 971 I	KIQNFRVYYR	KIQNFRVYYR	<u>79</u>	133	6	20	49	4	3
					 				
						- 1	0.7	_	<u> </u>
Pol 347	AIFQSSMTK	AIFQSSMTK	<u>80</u>	88	5	17	27	3	2
		A TROCCHETY	145	1.0		2	-		
		AIFQCSMTK	145	19		1	5 11		1
		AIFQSSMTR	146	9	-				<u> </u>
		AIFQASMTK	147	9	3		6		
		SIFQSSMTK	148	4	3		l °		
		AIFQYSMTK	149	2			1		
		AIFQSTMTK	150				-		
Del 700 "	TOUT NUMBER OF	KVYLSWVPAHK	161	56	8		12	1	3
Pol 722 K	VYLAWVPAHK	VAITDMALWUY	<u>151</u>	ا عو			12	1	3
		RVYLSWVPAHK	152	55			41		
		KVYLAWVPAHK	81	23	1	18		3	

		VPFQLPPI	178	26			23		1
		VPLQLPPI	177	34	2	1	19		
Rev 75	VPLQLPPL	VPLQLPPL	85	64	5	15	7	4	2
		YPPLTSLKSL	175	6					-
		YPLTSLRSLF	174	6	-	4	-		-
•		YPPLASLKSL	173	10 6		4			
		YPLTSLKSLF	172	10	ļ	1		2	1
		YPLASLRSLF	84	11		10			-
π	maximal populat		0.4	1 11	T	10			1
		d not be predic	ted to XI	R. Would	cho	ose :	both	to	get
		YPLASLKSLF*	<u>2</u> .	13		5		2	
Gag 545	YPLASLRSLF	EPLTSLKSLF*	1	22			21		
		111112		-					-
		FPVRPQVPL	168	4	+		2		
		FPVKPQVPL	167	9	1	3	2		-
Nef 94	FPVRPQVPL	FPVRPQVPL	83	135	8	17	51	4	3
		ATLFCASDAR	<u>165</u>	2	<u> </u>	-	2		
		TTLFCASEAK	164	2		1			<u> </u>
		TTLFCASDAR	163	2		2			<u> </u>
		PTLFCASDAK	162	2			1		
		TILFCASDAK	161	6					ļ
		ATLFCASDAK	<u>160</u>	7			7		
Env 61	TTLFCASDAK	TTLFCASDAK	82	121	9	19	41	4	1
		QVIBIWITAIR							
		QVYLTWVPAHK	158	2					ļ
		RIYLSWVPAHK KIYLAWVPAHK	157	2	 -	1			
		KIYLSWVPAHK	155 156	5 5		 	4		-
		KVYLTWVPAHK	154	5		2	3		

VPFQLPPL **IPIHYCAPA** Env 259 IPIHYCAPA IPIHYCTPA IPIHFCAPA **HPVHAGPIA** Gag 237 HPVHAGPIA HPVHAGPVA HPVQAGPVA

		HPIHAGPIA	186	2			2		
Pol 893	IPYNPQSQGVV	IPYNPQSQGVV	88	153	9	18	60	4	3
		IPYNPQSQGVI	188	5		3			
		IPYNPQSQGAV	189	2			1		
		,							
Env 250	CPKVSFEPI	CPKVSFEPI	89	50	5	17	3	2	0
		CPKVSFDPI	191	42			33		
		CPKVTFDPI	192	16			13		1
		CPKVTFEPI	193	13	3		1		1
		CPKISFDPI	194	9			5		
		CPKISFEPI	195	7		4		1	
		CPKVSWDPI	196	6					
		CPKVSFQPI	197	4		1			

^{*} The preferred epitopes are shown in bold

Table 9. Predicted immunological conservation for a panel of HLA-A2 restripeptides.

peptides.						1
Source	Parent	HPV	Variant	SEQ ID	Predicted	_Measured
	Sequence	Strain	Sequences	NO	Immunogenicity	Immunogeni city (SU)*
HPV16.E7.86	TLGIVCPI	16	TLGIVCPI	198	+	103.7
		18	TLSFVCPW	199	_	
		31	SFGIVCPN	200	-	
		33	TVNIVCPT	201	-	
		45	TLSFVCPW	199	_	
		52	TLQVVCPG	203	_	
	- · · · · · · · · · · · · · · · · · · ·	56	ALTVTCPL	204	_	
		58	TCTIVCPS	205	-	
HPV31.E6.11	KLHELSSAL	16	KLPQLCTEL	206	_	
		18	KLPDLCTEL	207	_	
		31	KLHELSSAL	208	+	26.3
		33	TLHDLCQAL	209	-	
		45	KLPDLCTEL	207	-	
	•	52	TLHELCEVL	211	-	
		56	SLHHLSEVL	212	-	
	•	58	TLHDLCQAL	209	-	
HPV18/45.E6	KLPDLCTEL	16	KLPQLCTEL	206	+	15.7
		18	KLPDLCTEL	210	+	212.7
		31	KLHELSSAL	208	-	
		33	TLHDLCQAL	209	-	
		45	KLPDLCTEL	207	+	205.1
		52	TLHELCEVL	211	-	
		56	SLHHLSEVL	212	-	
		58	TLHDLCQAL	209	-	
HPV52.E6.18	VLEESVHEI	16	ELQTTIHDI	222	_	
		18	ELNTSLQDI	223	-	
		31	ALEIPYDEL	224	-	
		33	ALETTIHNI	225	-	
		45	ELNTSLQDV	226	-	
		52	VLEESVHEI	227	+	64.1
		56	VLEIPLIDL	228	-	
		58	ALETSVHEI	229	_	
HPV18.E6.47	FAFKDLFVV	16	FAFRDLCIV	230		
		18	FAFKDLFVV	231	+	350.6
		31	FAFTDLTIV	232	-	
		33	FAFADLTVV	233	-	31.4
		45	FAFKDLCIV	234	-	176.9

		52	FLFTDLRIV	235		
		56	FACTELKLV	236	-	
		58	FVFADLRIV	237	_	7.7
HPV31.E6.45	FAFTDLTIV	16	FAFRDLCIV	230	-	
		18	FAFKDLFVV	231		
		31	FAFTDLTIV	232	+	20.7
		33	FAFADLTVV	233	+	11.6
		45	FAFKDLCIV	234	_	
		52	FLFTDLRIV	235	_	
		56	FACTELKLV	236	_	
		58	FVFADLRIV	237	_	
HPV52.E6.45	FLFTDLRIV	16	FAFRDLCIV	230	-	
		18	FAFKDLFVV	231	_	
		31	FAFTDLTIV	232	-	
		33	FAFADLTVV	233	-	
		45	FAFKDLCIV	234	_	
		52	FLFTDLRIV	235	+	421.4
		56	FACTELKLV	236		57.5
		58	FVFADLRIV	237	+	94.1
		30	TVIPADBRIV	237	•	
HPV58.E6.45	FVFADLRIV	16	FAFRDLCIV	230	-	
		18	FAFKDLFVV	231	-	
		31	FAFTDLTIV	232	_	
		33	FAFADLTVV	233	-	
		45	FAFKDLCIV	234	-	
		52	FLFTDLRIV	235	+	13.3
		56	FACTELKLV	236	_	21.0
		58	FVFADLRIV	237	+	62.8
HPV18.E7.7	TLQDIVLHL	16	TLHEYMLDL	262	-	
		18	TLQDIVLHL	263	+	99.0
		31	TLQDYVLDL	264	_	
		33	TLKEYVLDL	265		
		45	TLQEIVLHL	266	+	
		52	TIKDYILDL	267	<u> </u>	
		56	TLQDVVLEL	268	+	38.0
		58	TLREYILDL	269	-	
HPV16.E7.82	LLMGTLGIV	16	LLMGTLGIV	270	+	518.5
		18	LFLNTLSFV	271	-	
		31	LLMGSFGIV	272	+	90.1
		33	LLMGTVNIV	273	_	
		45	LFLSTLSFV	274	+	
		52	MLLGTLQVV	275		
		56	LLMGALTVT	276		· ·
		58	LLMGTCTIV	277	<u>-</u>	

******	TTMOMENT	1-16	T T MODIT OF TY	270	_	
HPV33.E7.81	LLMGTVNIV	16	LLMGTLGIV	270	-	
		18	LFLNTLSFV	271	-	
		31	LLMGSFGIV	272	- -	-
		33	LLMGTVNIV	273	+	179.4
		45	LFLSTLSFV	274	_	
		52	MLLGTLQVV	275	+	
		56	LLMGALTVT	276	_	20.8
		58	LLMGTCTIV	277	_	
HPV52.E7.84	MLLGTLQVV	16	LLMGTLGIV	270	_	
		18	LFLNTLSFV	271	-	
		31	LLMGSFGIV	272	-	
		33	LLMGTVNIV	273	+	
		45	LFLSTLSFV	274	-	
		52	MLLGTLQVV	275	+	99.8
		56	LLMGALTVT	276	=	
		58	LLMGTCTIV	277	-	
HPV56.E7.89	LLMGALTVT	16	LLMGTLGIV	270	-	
		18	LFLNTLSFV	271	-	
		31	LLMGSFGIV	272	-	
		33	LLMGTVNIV	273	+	
		45	LFLSTLSFV	274	-	
		52	MLLGTLQVV	275	-	
		56	LLMGALTVT	276	+	263.5
		58	LLMGTCTIV	277	-	43.6

^{*} Immunogenicity was measured for all variants. Only the positive responses are shown in the table. All other responses were negative.

Table 10. 167 HIV-1 Variants

SEQ ID NO	Sequence Designation	Name	Accession Number	SubType	Country
	A.UG.92UG037 U51190	92UG037	U51190	Α	UG
	A.BY.97BL006 AF1932	97BL006	AF193275	Α	BY
	A.KE.Q23_AF004885	Q23	AF004885	Α	KE
	A.SE.SE6594_AF06967	SE6594	AF069672	Α	SE
	A.SE.SE7253_AF06967	SE7253	AF069670	Α	SE
	A.SE.SE7535_AF06967	SE7535	AF069671	Α	SE
	A.SE.SE8538_AF06966	SE8538	AF069669	Α	SE
	A.SE.SE8891_AF06967	SE8891	AF069673	Α	SE
	A.UG.U455_M62320	U455	M62320	Α	UG
	A.SE.UGSE8131_AF107	UGSE8131	AF107771	Α	SE
	A2.CY.94CY017.41_AF	94CY017.41	AF286237	A2	CY
	A2.CD.97CDKTB48_AF2	97CDKTB48	AF286238	A2	CD
	A2D97KR004_AF286	97KR004	AF286239	A2D	KR
	A2G.CD.97CDKP58_AF3	97CDKP58	AF316544	A2G	CD
	AC.IN.21301_AF06715	21301	AF067156	AC	IN
	AC.RW.92RW009_U8882	92RW009	U88823	AC	RW
	AC.SE.SE9488_AF0714	SE9488	AF071474	AC	SE
	ACD.SE.SE8603_AF075	SE8603	AF075702	ACD	SE
	ACG.BE.VI1035_AJ276	VI1035	AJ276595	ACG	BE
	AD.SE.SE6954_AF0757	SE6954	AF075701	AD	SE
	AD.SE.SE7108_AF0714	SE7108	AF071473	AD	SE
	ADHK.NO.97NOGIL3_AJ	97NOGIL3	AJ237565	ADHK	NO
	ADK.CD.MAL_X04415	MAL	X04415	ADK	CD
	AG.NG.92NG003_U8882	92NG003	U88825	AG	NG
	AG.BE.VI1197_AJ2765	VI1197	AJ276596	AG	BE
	AGHU.GA.VI354_AF076	VI354	AF076474	AGHU	GA
	AGU.CD.Z321_U76035	Z321	U76035	AGU	CD
	AJ.BW.BW2117_AF1921	BW2117	AF192135	ĄJ	BW
	B.NL.3202A21_U34604	3202A21	U34604	В	NL
	B.US.BC_L02317	BC	L02317	В	US
	B.GB.CAM1_D10112	CAM1	D10112	В	GB
	B.DE.D31_U43096	D31	U43096	В	DE
	B.US.DH123_AF069140	DH123	AF069140	В	US
	B.GB.GB8.C1_Y13716	GB8	AJ271445	В	GB
	B.DE.HAN_U43141	HAN	U43141	В	DE
	B.FR.HXB2_K03455	HXB2	K03455	В	FR
	B.US.JRCSF_M38429	JRCSF	M38429	В	US
	B.GB.MANC_U23487	MANC	U23487	В	GB
	B.US.MNCG_M17449	MNCG	M17449	В	US
	B.GA.OYI,_M26727	OYI	M26727	В	GA
	B.US.P896_U39362	P896	M96155	В	US
	B.US.RF_M17451	RF	M17451	B B	US
	B.CN.RL42_U71182	RL42	U71182	В	CN US
	B.US.SF2_K02007	SF2 TWCYS	K02007 AF086817	В	TW
	B.TW.TWCYS_AF086817	VH	AF146728	В	AU
	B.AU.VH_AF146728	WEAU160	U21135	В	US
	B.US.WEAU160_U21135 B.KR.WK_AF224507	WEAU160	AF224507	В	KR
	D.NN.WN_AF224301	VVIX	AI 224301	D	1313

B.US.WR27_U26546 WR27 U26546 B US B.US.YUZ_M93258 B US BF1.BR.93BR029.4_AF 93BR029.4 AF005495 BF1 BR C.BR.92BR025_U52953 92BR025 U52953 C BR C.IN.93IN101_AB0238 93IN101 AB023804 C IN C.IN.93IN999_AF0671 93IN999 AF067157 C IN C.IN.93IN999_AF0671 93IN999 AF067157 C IN C.IN.93IN999_AF0671 93IN999 AF067159 C IN C.IN.93IN399_AF06671 93IN999 AF067159 C IN C.IN.93IN399_AF06671 93IN3999 AF067155 C IN C.IN.93IN399_AF06671 93IN3999 AF067155 C IN C.IN.93IN399_AF06710 96BW0402 AF110962 C BW C.BW.96BW1210_AF110 96BW1210 AF110972 C BW C.BW.96BW1210_AF110 96BW1210 AF110972 C BW C.BW.96BW15803_AF11 96BW1210 AF110972 C BW C.ET.ETH2220_U46016 ETH2220 U46016 C ET C.BW.96BW16160_AF11 96BW111 AF110969 C BW C.BW.00BW0768.20_AF44 00BW0768.21 AF443088 C BW C.BW.00BW0768.20_AF44 00BW0768.21 AF443089 C BW C.BW.00BW0768.20_AF44 00BW0768.20 AF443099 C BW C.BW.00BW1471.27_AF44 00BW1471.27 AF443091 C BW C.BW.00BW1616.2_AF44 00BW166.2 AF443091 C BW C.BW.00BW17793_AF44 00BW17593_AF443091 C BW C.BW.00BW17793_AF44 00BW1768.8 AF443092 C BW C.BW.00BW17793_AF44 00BW1768.8 AF443093 C BW C.BW.00BW17795_3_AF44 00BW17693_AF443094 C BW C.BW.00BW17795_AF44 00BW17693_AF443094 C BW C.BW.00BW17795_AF44 00BW1783_5 AF443096 C BW C.BW.00BW1783_5_AF44 00BW1783_5 AF443099 C BW C.BW.00BW1891_3_AF44 00BW1783_5 AF443099 C BW C.BW.00BW1891_3_AF44 00BW1783_5 AF443096 C BW C.BW.00BW1891_3_AF44 00BW1881_3 AF443101 C BW C.BW.00BW2083_6_AF44 00BW1881_3 AF443101 C BW C.BW.00BW208_6_AF44 00BW1881_3 AF443101 C BW C.BW.00BW208_6_AF44 00BW3881_3 AF443101 C BW C.BW.00BW208_6_AF44 00BW208_6_A AF443100 C BW C.BW.00BW208_6_AF44 00BW208_6_A AF443100 C BW C.BW.00BW208_6_AF44 00BW3881_3 AF443101 C BW C.BW.00BW3881_3_AF44 00BW3881_3 AF443100 C BW C.BW.00BW3881_3_AF44					
B.U.S.YUZ M93258	B US WR27 U26546	WR27	U26546	В	US
BF1 BR SER029 A AF					
C.BR. 92BR025 U52953 C.BR C.IN.93IN101_AB0238 93IN101 AB023804 C.IN. C.IN.93IN904_AF0671 93IN994 AF067157 C.IN. C.IN.93IN990_AF0671 93IN999 AF067154 C.IN. C.IN.93IN999_AF0671 93IN999 AF067154 C.IN. C.IN.93IN999_AF0671 93IN999 AF067155 C.IN. C.IN.94IN11246_AF06 94IN11246 AF067155 C.IN. C.IN.95IN21068_AF06 95IN21068 AF067155 C.IN. C.IN.95IN21068_AF06 95IN21068 AF067155 C.IN. C.IN.95IN21068_AF110 96BW0402 AF110972 C.BW. C.BW.96BW1510_AF110 96BW15803 AF110972 C.BW. C.BW.96BW1510_AF111 96BW15803 AF110973 C.BW. C.BW.96BW11B01_AF11 96BW15803 AF110973 C.BW. C.BW.00BW0762.1_AF44 00BW0762.1 AF443088 C.BW. C.BW.00BW0762.1_AF44 00BW0762.1 AF443088 C.BW. C.BW.00BW0762.1_AF44 00BW0762.1 AF443099 C.BW. C.BW.00BW0764.21_AF44 00BW0874.21 AF443090 C.BW. C.BW.00BW174.27_AF44 00BW0874.21 AF443090 C.BW. C.BW.00BW1616.2_AF44 00BW1616.2 AF443092 C.BW. C.BW.00BW1616.2_AF44 00BW1616.2 AF443092 C.BW. C.BW.00BW1783_AF44 00BW1773.2 AF443093 C.BW. C.BW.00BW1783_AF44 00BW1783.5 AF443094 C.BW. C.BW.00BW1783.5_AF44 00BW1783.5 AF443095 C.BW. C.BW.00BW1783.5_AF44 00BW1783.5 AF443095 C.BW. C.BW.00BW1783.5_AF44 00BW1783.5 AF443095 C.BW. C.BW.00BW1880.2_AF44 00BW1880.2 AF443100 C.BW. C.BW.00BW1880.2_AF44 00BW1880.2 AF443100 C.BW. C.BW.00BW2083.6_AF44 00BW1880.2 AF443100 C.BW. C.BW.00BW218.3_AF44 00BW1880.2 AF443100 C.BW. C.BW.00BW218.3_AF44 00BW1880.2 AF443100 C.BW. C.BW.00BW386.8_AF44 00BW2086.6 AF443100 C.BW. C.BW.00BW386.8_AF44 00BW2086.1 AF443100 C.BW. C.BW.00BW386.8_AF44 00BW386.8 AF443110 C.BW. C.BW.00BW386.8_AF44 00BW386.8 AF443110 C.BW. C.BW.00BW386.8_AF44 00BW386.8 AF443110 C.BW. C.BW.00BW386.8_AF44 00BW386.8 AF443110 C.BW. C.B	—				
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C.BW.00BW1880.2_AF44	C.BW.00BW1811.3_AF44	00BW1811.3		С	
C.BW.00BW1921.13_AF44	C.BW.00BW1859.5 AF44	00BW1859.5	AF443099	С	BW
C.BW.00BW1921.13_AF44	C BW.00BW1880.2 AF44	00BW1880.2	AF443100	С	BW
C.BW.00BW2036.1_AF44	-			Č	
C.BW.00BW2063.6_AF44				Č	
C.BW.00BW2087.2_AF44	-				
C.BW.00BW2127.214_AF44	—				
C.BW.00BW2128.3_AF44	C.BW.00BW2087.2_AF44	00BW2087.2	AF443104		BW
C.BW.00BW2128.3_AF44	C.BW.00BW2127.214 AF44	00BW2127.214	AF443105	С	BW
C.BW.00BW2276.7_AF44 00BW2276.7 AF443107 C C.BW.00BW3819.3_AF44 00BW3819.3 AF443108 C C.BW.00BW3842.8_AF44 00BW3842.8 AF443109 C C.BW.00BW3871.3_AF44 00BW3871.3 AF443110 C C.BW.00BW3876.9_AF44 00BW3876.9 AF443111 C C.BW.00BW3886.8_AF44 00BW3886.8 AF443112 C C.BW.00BW3891.6_AF44 00BW3891.6 AF443113 C C.BW.00BW3891.6_AF44 00BW3891.6 AF443113 C C.BW.00BW3970.2_AF44 00BW3970.2 AF443114 C C.BW.00BW3970.2_AF44 00BW5031.1 AF443115 C C.BW.96BW01B21_AF11 96BW01B21 AF110960 C C.BW.96BW0407_AF11 96BW0407 AF110963 C C.BW.96BW0502_AF11 96BW0407 AF110963 C C.BW.96BW0502_AF11 96BW0502 AF110967 C C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C C.BW.96BW11.06_AF11 96BW11.06 AF110970 C C.BW.96BW1210_AF11 96BW1210 AF110970 C C.BW.96BW15B03_AF11 96BW15B03 AF110973 C C.BW.96BW15B03_AF11 96BW15B03 AF110973 C C.BW.96BW15B03_AF11 96BW15B03 AF110978 C C.BW.96BW17A09_AF11 96BW17A09 AF110979 C C.BW.96BWM01.5_AF44 96BWM01.5 AF443074 C C.BW.96BWM01.5_AF44 96BWM01.5 AF443074 C C.BW.96BWM03.2_AF44 96BWM03.2 AF443075 C C.BW.96BWM03.2_AF44 96BWM		00BW2128 3	AF443106	С	BW
C.BW.00BW3819.3_AF44 00BW3819.3 AF443108 C C.BW.00BW3842.8_AF44 00BW3842.8 AF443109 C C.BW.00BW3871.3_AF44 00BW3871.3 AF443110 C C.BW.00BW3876.9_AF44 00BW3876.9 AF443111 C C.BW.00BW3886.8_AF44 00BW3886.8 AF443112 C C.BW.00BW3891.6_AF44 00BW3891.6 AF443113 C C.BW.00BW3891.6_AF44 00BW3891.6 AF443113 C C.BW.00BW3970.2_AF44 00BW3970.2 AF443114 C C.BW.00BW3970.2_AF44 00BW3970.2 AF443115 C C.BW.96BW01B21_AF11 96BW01B21 AF110960 C C.BW.96BW0407_AF11 96BW0407 AF110963 C C.BW.96BW0502_AF11 96BW0502 AF110967 C C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C C.BW.96BW11.06_AF11 96BW11.06 AF110970 C C.BW.96BW1210_AF11 96BW1210 AF110972 C C.BW.96BW15B03_AF11 96BW15B03 AF110973 C C.BW.96BW15B03_AF11 96BW15B03 AF110973 C C.BW.96BW15B03_AF11 96BW15B03 AF110973 C C.BW.96BW17A09_AF11 96BW17A09 AF110979 C C.BW.96BWM01.5_AF44 96BWM01.5 AF443074 C C.BW.96BWM03.2_AF44 96BWM03.2 AF443075 C C.BW.96BWM03.2_AF44	—				
C.BW.00BW3842.8_AF44	—				
C.BW.00BW3871.3_AF44				Č	
C.BW.00BW3876.9_AF44	—				
C.BW.00BW3876.9_AF44	C.BW.00BW3871.3 AF44	00BW3871.3	AF443110	С	BW
C.BW.00BW3886.8_AF44		00BW3876.9	AF443111	С	BW
C.BW.00BW3891.6_AF44 00BW3891.6 AF443113 C BW C.BW.00BW3970.2_AF44 00BW3970.2 AF443114 C BW C.BW.00BW5031.1_AF44 00BW5031.1 AF443115 C BW C.BW.96BW01B21_AF11 96BW01B21 AF110960 C BW C.BW.96BW0407_AF11 96BW0407 AF110963 C BW C.BW.96BW0502_AF11 96BW0502 AF110967 C BW C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C BW C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
C.BW.00BW3970.2_AF44 00BW3970.2 AF443114 C BW C.BW.00BW5031.1_AF44 00BW5031.1 AF443115 C BW C.BW.96BW01B21_AF11 96BW01B21 AF110960 C BW C.BW.96BW0407_AF11 96BW0407 AF110963 C BW C.BW.96BW0502_AF11 96BW0502 AF110967 C BW C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C BW C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW17A09_AF11 96BW16.26 AF110978 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
C.BW.00BW5031.1_AF44 00BW5031.1 AF443115 C BW C.BW.96BW01B21_AF11 96BW01B21 AF110960 C BW C.BW.96BW0407_AF11 96BW0407 AF110963 C BW C.BW.96BW0502_AF11 96BW0502 AF110967 C BW C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C BW C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BWMO1.5_AF14 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
C.BW.96BW01B21_AF11 96BW01B21 AF110960 C BW C.BW.96BW0407_AF11 96BW0407 AF110963 C BW C.BW.96BW0502_AF11 96BW0502 AF110967 C BW C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C BW C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
C.BW.96BW0407_AF11 96BW0407 AF110963 C BW C.BW.96BW0502_AF11 96BW0502 AF110967 C BW C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C BW C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW	C.BW.00BW5031.1_AF44	00BW5031.1	AF443115		BW
C.BW.96BW0407_AF11 96BW0407 AF110963 C BW C.BW.96BW0502_AF11 96BW0502 AF110967 C BW C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C BW C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW	C.BW.96BW01B21 AF11	96BW01B21	AF110960	С	BW
C.BW.96BW0502_AF11 96BW0502 AF110967 C BW C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C BW C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
C.BW.96BW06.J4_AF29 96BW06.J4 AF290028 C BW C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW	- -				
C.BW.96BW11.06_AF11 96BW11.06 AF110970 C BW C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
C.BW.96BW1210_AF11 96BW1210 AF110972 C BW C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW	-				
C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW	C.BW.96BW11.06_AF11	96BW11.06	AF110970		BW
C.BW.96BW15B03_AF11 96BW15B03 AF110973 C BW C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW	C.BW.96BW1210 AF11	96BW1210	AF110972	С	BW
C.BW.96BW16.26_AF11 96BW16.26 AF110978 C BW C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW	<u>—</u>				
C.BW.96BW17A09_AF11 96BW17A09 AF110979 C BW C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
C.BW.96BWMO1.5_AF44 96BWMO1.5 AF443074 C BW C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
C.BW.96BWMO3.2_AF44 96BWMO3.2 AF443075 C BW					
	_				
C.BW.98BWMC12.2_AF44 98BWMC12.2 AF443076 C BW	C.BW.96BWMO3.2_AF44	96BWMO3.2	AF443075		BW
	C.BW.98BWMC12.2 AF44	98BWMC12.2	AF443076	С	BW

C.BW.98BWMC13.4 AF44	98BWMC13.4	AF443077	С	BW
C.BW.98BWMC14.a3 AF44	98BWMC14.a3	AF443078	С	BW
C.BW.98BWMO14.10_AF44	98BWMO14.10	AF443079	Č	BW
C.BW.98BWMO18.d5_AF44	98BWMO18.d5	AF443080	C	BW
C.BW.98BWMO36.a5_AF44	98BWMO36.a5	AF443081	С	BW
C.BW.98BWMO37.d5_AF44	98BWMO37.d5	AF443082	С	BW
C.BW.99BW3932.12_AF44	99BW3932.12	AF443083	С	BW
C.BW.99BW4642.4_AF44	99BW4642.4	AF443084	С	BW
C.BW.99BW4745.8_AF44	99BW4745.8	AF443085	Ċ	BW
	99BW4754.7	AF443086	Č	BW
C.BW.99BW4754.7_AF44			Č	
C.BW.99BWMC16.8_AF44	99BWMC16.8	AF443087		BW
CRF01_AE.CF.90CF11697_	90CF11697	AF197340	CRF01_AE	CF
CRF01_AE.CF.90CF402_U5	90CF402	U51188	CRF01_AE	CF
CRF01_AE.CF.90CF4071_A	90CF4071	AF197341	CRF01_AE	CF
CRF01 AE.TH.93TH057 AF	93TH057	AF197338	CRF01_AE	TH
CRF01_AE.TH.93TH065_AF	93TH065	AF197339	CRF01_AE	TH
CRF01_AE.TH.93TH253_U5	93TH253	U51189	CRF01_AE	TH
CRF01_AE.TH.95TNIH047_	95TNIH047	AB032741	CRF01_AE	TH
<u> </u>	CM240	U54771	CRF01_AE	TH
CRF01_AE.TH.CM240_U547			_	
CRF01_AE.TH.TH022_AB03	TH022	AB032740	CRF01_AE	TH
CRF02_AG.SN.98SEMP1211	98SEMP1211	AJ251056	CRF02_AG	SN
CRF02_AG.FR.DJ263_AF06	DJ263	AF063223	CRF02_AG	FR
CRF02_AG.FR.DJ264_AF06	DJ264	AF063224	CRF02_AG	FR
CRF02 AG.GH.G829 AF184	G829	AF184155	CRF02_AG	GH
CRF02 AG.NG.IBNG L3910	IBNG	L39106	CRF02 AG	NG
CRF02_AG.SE.SE7812_AF1	SE7812	AF107770	CRF02 AG	SE
CRF03 AB.RU.KAL153-2_A	KAL153-2	AF193276	CRF03_AB	RU
		AF193277	CRF03_AB	RU
CRF03_AB.RU.RU98001_AF	RU98001			
CRF04_cpx.CY.94CY032-3	94CY032-3	AF049337	CRF04_cpx	CY
CRF04_cpx.GR.97PVCH_AF	97PVCH	AF119820	CRF04_cpx	GR
CRF04_cpx.GR.97PVMY_AF	97PVMY	AF119819	CRF04_cpx	GR
CRF05_DF.BE.VI1310_AF1	VI1310	AF193253	CRF05_DF	BE
CRF05_DF.BE.VI961_AF07	VI961	AF076998	CRF05_DF	BE
CRF06 cpx.ML.95ML127_A	95ML127	AJ288982	CRF06_cpx	ML
CRF06 cpx.ML.95ML84_AJ	95ML84	AJ245481	CRF06_cpx	ML
CRF06_cpx.SN.97SE1078_	97SE1078	AJ288981	CRF06 cpx	SN
CRF06_cpx.AU.BFP90_AF0	BFP90	AF064699	CRF06_cpx	AU
CRF11_cpx.CM.97CM-MP81	97CM-MP818	AJ291718	CRF11_cpx	СМ
CRF11 cpx.GR.GR17_AF17	GR17	AF179368	CRF11_cpx	GR
<u> </u>		U88822	D	CD
D.CD.84ZR085_U88822	84ZR085			
D.UG.94UG1141_U8882	94UG1141	U88824	D	UG
D.CD.ELI_K03454	ELI	K03454	D	CD
D.CD.NDK_M27323	NDK	M27323	D	CD
F1.BR.93BR020.1_AF0	93BR020.1	AF005494	F1	BR
F1.FI.FIN9363 AF075	FIN9363	AF075703	F1	FI
F1.FR.MP411 AJ24923	MP411	AJ249238	F1	FR
F1.BE.VI850 AF07733	VI850	AF077336	F1	BE
F2.CM.MP257_AJ24923	MP257	AJ249237	F2	СМ
F2KU.BE.VI1126_AF07	VI1126	AF076475	F2KU	BE
			G	
G.NG.92NG083_U88826	92NG083	U88826		NG BE
G.BE.DRCBL_AF084936	DRCBL	AF084936	G	BE
G.SE.SE6165_AF06164	SE6165	AF061642	G	SE
H.CF.90CF056_AF0054	90CF056	AF005496	H	CF
H.BE.VI991_AF190127	VI991	AF190127	Н	BE

H.BE.VI997 AF190128	VI997	AF190128	Н	BE
J.SE.SE7022_AF08239	SE7022	AF082395	Ĵ	SE
J.SE.SE7887 AF08239	SE7887	AF082394	J	SE
K.CD.EQTB11C_AJ2492	EQTB11C	AJ249235	K	CD
K.CM.MP535_AJ249239	MP535	AJ249239	K	CM
N.CM.YBF30 AJ006022	YBF30	AJ006022	Ν	CM
O.SN.99SE-MP1299_ZX	SEMP1299	AJ302646	0	- SN
O.SN.99SE-MP1300_ZX	SEMP1300	AJ302647	0	SN
O.CM.ANT70_L20587	ANT70	L20587	0	CM
O.CM.MVP5180_L20571	MVP5180	L20571	0	CM
U.CD83CD0031	83CD0031	AF286236	U	CD

Table 11. HIV Gag Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

Mama	0.00000763 1	CEO TO NO.	202	Ton.	EE6	Choole.	2512	Weight:	1.00
Name:		SEQ ID NO:				Check:		_	1.00
Name:	_			Len:	556	Check:		Weight:	
Name:	_	SEQ ID NO:		Len:	556	Check:		Weight:	1.00
Name:	_		305		556	Check:		Weight:	1.00
Name:	00BW1616_2	SEQ ID NO:		Len:	556	Check:		Weight:	1.00
Name:	00BW1686_8	SEQ ID NO:	307	Len:	556	Check:	7822	Weight:	1.00
Name:	00BW1759_3	SEQ ID NO:	308	Len:	556	Check:	7777	Weight:	1.00
Name:	00BW1773_2	SEQ ID NO:	309	Len:	556	Check:	9727	Weight:	1.00
Name:	00BW1783_5	SEQ ID NO:	310	Len:	556	Check:	9681	Weight:	1.00
Name:	00BW1795_6	SEQ ID NO:	311	Len:	556	Check:	9667	Weight:	1.00
Name:	00BW1811 3	SEQ ID NO:	312	Len:	556	Check:	4422	Weight:	1.00
Name:	00BW1859 5	SEO ID NO:	313	Len:	556	Check:	7320	Weight:	1.00
Name:	- .		314	Len:	556	Check:	1603	Weight:	1.00
Name:	00BW1921 1		315	Len:	556	Check:	883	Weight:	1.00
Name:	00BW2036 1			Len:	556	Check:		Weight:	1.00
Name:	00BW2063 6			Len:	556	Check:		Weight:	1.00
Name:				Len:	556	Check:		Weight:	1.00
	_			Len:	556	Check:		Weight:	1.00
Name:	-		320		556	Check:		Weight:	1.00
Name:	_							_	
Name:				Len:	556	Check:		Weight:	1.00
Name:	_	SEQ ID NO:	322	Len:	556	Check:		Weight:	1.00
Name:	00BW3842_8			Len:	556	Check:		Weight:	1.00
Name:	00BW3871_3	SEQ ID NO:	324	Len:	556	Check:		Weight:	1.00
Name:	00BW3876_9	SEQ ID NO:	325	Len:	556	Check:		Weight:	1.00
Name:	00BW3886_8	SEQ ID NO:	326	Len:	556	Check:		Weight:	1.00
Name:	00BW3891_6	SEQ ID NO:	327	Len:	556	Check:	129	Weight:	1.00
Name:	00BW3970_2	SEQ ID NO:	328	Len:	556	Check:	8768	Weight:	1.00
Name:	00BW5031 1	SEQ ID NO:	329	Len:	556	Check:	3966	Weight:	1.00
Name:	96BW01B21	SEQ ID NO:	330	Len:	556	Check:	602	Weight:	1.00
Name:	96BW0407	SEQ ID NO:	331	Len:	556	Check:	9836	Weight:	1.00
Name:	96BW0502	SEQ ID NO:	332	Len:	556	Check:	6402	Weight:	1.00
Name:		SEQ ID NO:		Len:	556	Check:	254	Weight:	1.00
Name:		SEQ ID NO:		Len:	556	Check:	6801	Weight:	1.00
Name:	96BW1210	SEQ ID NO:		Len:	556	Check:		Weight:	1.00
Name:		SEQ ID NO:		Len:	556	Check:		Weight:	1.00
Name:		SEQ ID NO:		Len:	556	Check:		Weight:	1.00
	_		338	Len:	556	Check:		Weight:	1.00
Name:						Check:		_	1.00
Name:	-	SEQ ID NO:	339		556	Check:		Weight:	
	96BWMO3_2	SEQ ID NO:	340		556			Weight:	1.00
	98BWMC12_2	SEQ ID NO:		Len:	556	Check:		Weight:	1.00
Name:				Len:	556	Check:		Weight:	1.00
Name:				Len:		Check:		Weight:	1.00
		SEQ ID NO:				Check:		Weight:	1.00
	98BWM018_d		345	Len:		Check:		Weight:	1.00
Name:	98BWMO36_a		346	Len:	556	Check:	4386	Weight:	1.00
Name:	98BWMO37_d	SEQ ID NO:	347	Len:	556	Check:	6900	Weight:	1.00
Name:	99BW3932 1	SEQ ID NO:	348	Len:	556	Check:	292	Weight:	1.00
Name:	99BW4642_4	SEQ ID NO:	349	Len:	556	Check:	1347	Weight:	1.00
	99BW4745 8				556	Check:	7980	Weight:	1.00
	99BW4754 7			Len:		Check:		Weight:	1.00
Name:	. - .		352		556	Check:		Weight:	1.00
Name:	· - - -		353			Check:		Weight:	1.00
Name:				Len:	556	Check:		Weight:	1.00
Name:				Len:	556	Check:		Weight:	1.00
Name:	A2G CD 97C			Len:		Check:		Weight:	1.00
			357	Len:	556	Check:		Weight:	1.00
Name:	A_BY_97BL0	PEC ID NO:		nem;	000	CITCUR.	,,,,		

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Check: 2442
Name: A_KE_Q23_A SEQ ID NO: 358 Len: 556
                                                         Weight:
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B US WR27
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AC_IN_2130	AGTTSTLQEQ	IAWMTG.NPP	VPVGEIYKRW	IILGLNKIVR	MYSPVSILDI
AC_RW_92RW	AGTTSTLQEQ	IAWMTN.NPP	IPVGEIYKRW	IILGLNKIVR	MYSPVSILDI
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ACD_SE_SE8	AGTTSTLQEQ	IAWMTS.NPP	IPVGDIYKRW	IILGLNKIVR	MYSPVSILDI
ACG_BE_VI1	AGTTSTLQEQ	IGWMTS.NPP	IPVGEIYKRW	IILGLNKIVR	MYSPVSILDI
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ADHK_NO_97	AGTTSTLQEQ	IGWMTS.NPP	IPVGEIYKRW	IILGLNKIVR	MYSPVSILDI
ADK CD MAL	AGTTSTLQEQ	IGWMTS.NPP	IPVGDIYKRW	IILGLNKIVR	MYSPVSILDI
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B FR HXB2	AGTTSTLQEQ	IGWMTN.NPP	IPVGEIYKRW		MYSPTSILDI
B GA OYI	AGTTSTLOEO	IGWMTN.NPP	IPVGEIYKRW		MYSPTSILDI
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B_GB_MANC_	AGTTSTLQEQ		IPVGEIYKRW		MYSPASILDI
B_KR_WK_AF	AGTTSTLQEQ	IGWMTN.NPP			MYSPTSILDI
B_NL_3202A	AGTTSTLQEQ	IGWMTH.NPP	IPVGEIYKRW		MYSPTSILDI
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B_US_BC_L0	AGTTSTLQEQ	IGWMTN.NPP	IPVGEIYKRW		MYSPSSILDI
B_US_DH123	AGTTSTLQEQ	IGWMTN.NPP	IPVGEIYKRW		MYSPTSILDI
B_US_JRCSF	AGTTSTLQEQ	IGWMTN.NPP	IPVGEIYKRW		MYSPVSILDI
B_US_MNCG_	AGTTSTLQEQ	IGWMTN.NPP	IPVGEIYKRW		MYSPSSILDI
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C_IN_93IN1	AGTTSSLQEQ	IAWMTG.NPP	VPVGDIYKRW	IILGLNKIVR	MYSPVSILDI
C IN 93IN9	AGTTSSLQEQ	IAWMTG.NPP	VPVGDIYKRW	IILGLNKIVR	MYSPVSILDI
C IN 93IN9	AGTTSTLQEQ	IAWMTG.NPP	VPVGDIYKRW	IILGLNKIVR	MYSPVSILDI
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B US SF2 K GNFRNQRKTV KCFNCGKEGH IAKNCRAPRK KGCWRCGREG HQMKDCTE..
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K CM MP535
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          ACD SE SE8
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RQANFLGKIW PSHKG.RPGN FLQ...... SRPEP TAPPAESFR.
C BW 96BW0
C BW 96BW1
           RRANFLGKIW PSHKG.RPGN FLQSRPE... .....P TAPPAESF..
           GQANFLGKIW PSHKG.RPGN FLQSR..... PEP SAPPAESFR.
C BW 96BW1
           RQANFLGKIW PSHKG.RPGN FLQNRTEP...... TAPPAESFK.
C BW 96BW1
           RQANFLGRLW PSNKG.RPGN FLQSRP.... EP TAPPESLRPE
C ET ETH22
           RQANFLGKIW PSHKG.RPGN FLQ......SRPEP TAPPAESFR.
C IN 93IN1
C IN 93IN9
           ROANFLGKIW PSHKG.RPGN FLQ...... SRPEP TAPPAESFR.
C IN 93IN9
           RQANFLGKIW PSHKG.RPGN FLQNRPEPTA PP...ARPEP TAPPAESFR.
C IN 94IN1
           ROANFLGKIW PSHKG.RPGN FLQ...... SRPEP TAPPAESFR.
           RQANFLGKIW PSHKG.RPGN FLQ...... SRPEP TAPPAESFR.
C IN 95IN2
CRF01 AE C
           RQANFLGKIW PLNKG.RPGN FPQSRLE... .....PT APPA.ESLG.
CRF01_AE C
           RQANFLGKIW PSSKG.RPGN FPQSRPE.......PT APPM.ESLG.
CRF01_AE C
           RQANFLGRIW PSSKG.RPGN FPQSRPE... .....PT APPA.ESLG.
CRF01 AE T
           RQANFLGKFW PSNKG.RPGN FPQSRPE........PT APPA.ENWG.
CRF01 AE T
           RQANFLGKIW PSNKG.RPGN FPQSRPE........PT APP..AEWG.
CRF01_AE T
           RQANFLGKIW PSNKG.RPGN FPQSKPE........PT APPA.ENWG.
CRF01_AE_T
           RQANFLGKIW PSNKG.RPGN FPQSRPE.......PT APPA.ENWG.
CRF01_AE_T
           RQANFLGKIW PSNKG.RPGN FPQSRPE... .....PT APPA.ENWG.
CRF01_AE_T
           RQANFLGKIW PSNKG.RPGN FPQSRPE... .....PT APPA.ENWG.
           GQANFLGKIW PSSKG.RPGN FPQSRPE........PT APPA.ESLG.
CRF02_AG_F
           RQANFLGKIW PSSKG.RPGN FPQSRPE... .....PT APPA.ESFG.
CRF02_AG_F
CRF02_AG_G
           RQANFLGKIW PSNKG.RPGN FPQSRPE... P...... SAPPAESFG.
CRF02_AG_N
           RQANFLGKIW PSSKG.RPGN FPQSRPE.....PT APPA.ESFG.
           RQANFLGKIW PSSKG.RPGN FPQSRPE........PT APPA.ESLG.
CRF02_AG_S
CRF02 AG S
           RQANFLGKIW PSSKG.RPGN FPQSRPE.....PT APPA.ESFG.
           RQANFLGRIW PSSKG.RPGN FPQSRPE... .....PS APP.AENFG.
CRF03 AB R
           RQANFLGKIW PSSKG.RPGN FPQSRPE........PS APP.AENFG.
CRF03_AB_R
           RQANFLGRMW PSSKG.RPGN FLQNRPE.....PT APPA.ECLE.
CRF04_cpx_
           RQANFLGRMW PSSKG.RPGN FLQSRPE........PT APPA.ESLE.
CRF04 cpx
           RQANSLGRMW PSSKG.RPGN FLQSRTE... .....PT APPA.ESFE.
CRF04 cpx
           RQANFLGKVW PSHKG.RPGN FLQSRP.... EP SAPPAESFR.
CRF05 DF B
CRF05 DF B
           GQANFLGRVW LSHKG.RPGN FLQSRP.... EP SAPPAESFG.
           RQANFLGKIW PSNKG.RPGN FLQNRPE... .....P TAPPIESFG.
CRF06 cpx
           RQANFLGKIW PSNKG.RPGN FLQNRPE... .....P TAPPAESFG.
CRF06 cpx
CRF06_cpx_
           RQANFLGRIW PSSKG.RPGN FLQNRPE... .....P TAPPAESFG.
           RQANFLGKIW PSHKG.RPGN FLQNRPEQNR P.....EP SAPPAESFG.
CRF06_cpx_
CRF11_cpx_
           RQANFLGKIW PSSKG.RPGN FLQSRPE... .....PT APPA.ESFG.
CRF11_cpx_
           RQANFLGKIW PSSKG.RPGN FLQSRPE... .....PT APPA.ESFG.
           RQANFLGKIW PSHKG.RPGN FLQSRPE... .....P TAPPAE.FG.
D CD 84ZR0
           RQANFLGRIW PSHKG.RPGN FLQSRP.... EP TAPPAESFG.
D_CD_ELI_K
D CD NDK M
           RQANFLGKIW PSHKG.RPGN FLQSRP.... EP TAPPAESFG.
D UG 94UG1
           RQANFLGKIW PSHNG.RPGN FLQSRPPA.. .....EP TAPPAEIFG.
           RQANFLGKIW PSNKG.RPGN FLQSRPE... .....P TAPPAESFG.
F1 BE VI85
           RQANFLGKIW PSNKG.RPGN FIQNRPE... .....P SAPPAESFR.
F1 BR 93BR
           RQANFLGKIW PSNKG.RPGN FLQSRPE.... ..........P TAPPAESLG.
F1 FI FIN9
           RQANFLGKIW PSNKG.RPGN FLQNRPE... .....P TAPPAESFG.
F1 FR MP41
           RQANFLGKMW PSNKG.RPGN FLQNRPE... .....P TAPPAESFG.
F2 CM MP25
           RQANFLGKIW PSNKG.RPGN FLQSRPE... .....P TAPPAESFG.
F2KU BE VI
           RQANFLGKIW PSNKG.RPGN FLQNRPE.... P TAPPAENFG.
G BE DRCBL
           RQANFLGKIW PSNKG.RPGN FLQNRTE... .....P TAPPAESFG.
G NG 92NG0
           RQANFLGKIW PSNKG.RPGN FLQNRTE... .....P TAPPAESLG.
G_SE_SE616
           RQANFLGKIW PSSKG.RPGN FPQKRLE... .....P TAPPAESFG.
H_BE_VI991
H_BE_VI997
           RQANFLGKIW PSSKG.RPGN FLQSRPE... .....P TAPPAESFG.
H_CF_90CF0
           RQANFLGKIW PSSKG.RPGN FLQSRPE... .....P TAPPAESFG.
           RQANFLGKIW PSSKG.RPGN FLQSRPE... .....P TAPPAESLG.
J_SE_SE702
           RQANFLGKIW PSSKG.RPGN FLQSRPE.... P TAPPAESLG.
J_SE_SE788
           RQANFLGKFW PLNKE.RPGN FLQNRPE... .....P TAPPAESFG.
K CD EQTB1
K CM MP535
           RQANFLGKIW PSHKG.RPGN FLQSRPE... .....P TAPPAESFG.
N_CM_YBF30
           RQANFLGKSW SPFKG.RPGN FPQTTTRK.. .....EP TAPPLESYG.
O_CM_ANT70
           KQANFLGKYW PP.GGTRPGN YVQRPAH... ..... P SAPPMEEEVK
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0 91 191551			101010110	ъ	CADDMERAUZ
O_CM_MVP51	RQANFLGKYW	PP.GGTRPGN	YVQKQVS	P	SAPPMEEAVK
O_SN_99SE_	RQANFLGKYW	PP.GGTRPGN	YAQRQVS	Р	SAPPMTEEMK
O_SN_99SE_	KQANFLGKYW	PP.GGTRPGN	YAQRQVS	P	SAPPMTEEMK
U_CD83C	RQANFLGKIW	PSNKG.RPGN	FLQNRPE	P	TAPPAESFG.
	501				550
00BW0762_1	FE	ETNPTP	KQE	PKDRE	PLTSLKSLFG
00BW0768 2	FE	.ETTTPAP	KQE	LKDRE	PLTALKSLFG
00BW0874 2	FE	ETTPAL	KRE	LKERE	PLISLKSLFG
00BW1471 2	FE	ETTPAP	KQE	PKDRE	PLTSLKSLFG
00BW1616 2	F	.GETTPSP	RQE	AKDRE	PLISLKSLFG
00BW1686 8		ETTPAP		PKDRE	
00BW1759 3		ETTPAP	-	PKDRE	
00BW1773 2		ETTPAP		PKDRE	
00BW1783 5		ETTPVQ		TKDRE	
00BW1785_5 00BW1795_6		.EETTPSP		LKDKE	
00BW1793_0 00BW1811 3		ETTPAS		KKDRE	TLTSLRSLFG
_		ETTPAP	KQE	OKDRE	
00BW1859_5				PKDRE	
00BW1880_2		ETTPAP	KQE		PLTSLKSLFG
00BW1921_1		ETTPAP	~	PKDRE	
00BW2036_1		ETTPAP		LKDRE	
00BW2063_6		.EETTPAP		MKDKE	
00BW2087_2		ETTPAS		LKDRE	
00BW2127_2		ETTHAP	KQE	LKDRE	
00BW2128_3		ETTPAP		PKNRE	
00BW2276_7		ETTPEL		PKDRE	PLTSLKSLFG
00BW3819_3	FE	EITPAP	KQE	TKDRE	PLTSLKSLFG
00BW3842_8	FE	ETTPAP	KQE	PKDRGPY.RE	PLISLKSLFG
00BW3871_3	FE	ETTPVP	KQE	PTDRE	PLTSLKSLFG
00BW3876 9	FE	ETTPTL	KQE	LKDRE	PLTSLKSLFG
00BW3886 8	FE	ETTPVP	KQE	QKDRE	ALTSLKSLFG
00BW3891 6	FE	EITPVP	KQE	PKDRE	PLTSLKSLFG
00BW3970 2	FE	ETTPAP	KQE	PKDRE	PLISLKSLFG
00BW5031 1	FG	ETTPAP	KQE	MKERE	PLISLKSLFG
96BW01B21	FE	ETTPAP	KQE	PKDRE	PLTSLRSLFG
96BW0407	FE	ETTPGQ	KQE	SKDRE	TLTSLKSLFG
96BW0502		ETTPAP	KQE	PKDREPY.RE	PLTALRSLFG
96BW06 J4		ETTPAL		PKDKE	PLTSLKSPFG
96BW11 06		.EETTPAP		TKDRE	
96BW1210		ETTPAQ			
96BW15B03		ETTPAP			PLISLKSLFG
96BW16 26		ETTPAP			
96BW17A09		ETTPAP			
96BWMO1 5		.EETTPAP			
96BWMO1_3		.PTAPPAE			
		ETTPAS			
98BWMC12_2		.EETTPAP			
98BWMC13_4		ETTPAP			
98BWMC14_a					
98BWMO14_1		EPTAPPAES.			
98BWM018_d		ETTPAL			
98BWMO36_a		ETNLAP			
98BWMO37_d		ETTPAP			
99BW3932_1		ETTPAP			
99BW4642_4		ETTPAP			
99BW4745_8		GATPTP			
99BW4754_7		ETTPTQ			
99BWMC16_8		ETNPAP			
A2_CD_97CD		EEITSSL			
A2_CY_94CY		.MGEEITSSL			
A2D97KR		.MGEETTPLQ	KQELK	NREQHT	PAISLKSLFG

A2G CD 97C					
		MGEEIT	DOLK O E	OVDDE OVD	DOTOL VOLEC
A_BY_97BL0					
A_KE_Q23_A		MGEETV			
A_SE_SE659					
A_SE_SE725					
A_SE_SE753		MREEIA			
A SE SE853					
A SE SE889					
A SE UGSE8		MGEEIA	SPPK.QE	QNNP	PSVSLKSLFG
A UG 92UG0		MREEIV			
A UG U455		.MGEKMTSPA			
AC IN 2130		ETTPAL	KOE	QKDRE	PLTSLKSLFG
AC_RW 92RW		MGEEIASPL.			
		MGEETASPE.			
AC_SE_SE94					
ACD_SE_SE8		FGEEITP			
ACG_BE_VI1		KEDAIDSS			
AD_SE_SE69		FGEEIAP			
AD_SE_SE71					
ADHK NO 97		IGEEIT	SYQK.QE	QKDREPPP	PLVSLKSLFG
ADK CD MAL		FGEEIK			
AG BE VI11		MEEEIT			
AG_NG_92NG		FGEEIAP			
AGHU_GA_VI		FGEEIA		PREKER.Y	
		TKEEITS		PRDKELYP	
AGU_CD_Z32					
AJ_BW_BW21		FGEETA		GKDKEL.Y	
B_AU_VH_AF		FGEETTTP		PIDKELY	
B_CN_RL42_		FGEETTTP		PIDKELY	
B_DE_D31_U		FGEETATP		PIDKELY	
B_DE_HAN_U		FGEATAP	.SQKQE	PIDKELY	PLASLKSLFG
B FR HXB2		SGVETTTP	.PQKQE	PIDKELY	PLTSLRSLFG
B_GA_OYI		FGEETTTP	.PQKQE	PIDKGLY	PLTSLRSLFG
B_GB_CAM1_		FGEEKTTP	.SQKQE	PIDKELY	PLASLRSLFG
B GB GB8 A		FGGETTTP	.SQKQE	PINKEPY	PLASLRSLFG
B_GB_MANC_		FGEETTTP		PIDKELY	
B KR WK AF				PIDKELY	
B_NL_3202A				PRDKELY	
B TW TWCYS		FGEOTTTP		PIDKDLY	
		FGEETTTP		DKEMY	
B_US_BC_L0				PKELY	
B_US_DH123		FGEETATP			
B_US_JRCSF		FGEETATP		PIDKELY	
B_US_MNCG_				TIDKDLY	
B_US_P896_		FGEETTTP			
B_US_RF_M1		FGEETTP			
B_US_SF2_K				PIDKELY	
B US WEAU1	·			PIDKELY	
B US WR27		FGXETTTP	.SQKQE	PIDKELY	PLASLRSLFV
B US YU2 M		FGEETTTP			
BF1 BR 93B		FGEEVTTP			
C BR 92BR0		FGEETTTPS.			
C BW 96BW0	FE		KQE		
		.EETTPAP			
C_BW_96BW1					
C_BW_96BW1		ETTPAQ			
C_BW_96BW1		ETTPAP			
C_ET_ETH22		FEEATPSPK.			
C_IN_93IN1		ETTPAP			
C_IN_93IN9		ETPPAP			
C_IN_93IN9		ETTPAL			
C_IN_94IN1		ETPPAP			
C_IN_95IN2		ETTPAP			
CRF01_AE_C		MGEEIT	SFPK.QE	QKDKEHPS	PLVSLKSLFG

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..... MGEEIT.... SFPK.Q...E QKDKK..QPP PLVSLKSLFG
CRF01 AE C
CRF01_AE C
           ..... MGEEIT.... SFSR.Q...E QKDRE..HPP PLVSLKSLFG
           ..... MGEETT.... .SLLKQ...E QKDKE..HHP PLVSLKSLFG
CRF01 AE T
           ..... MGEEIT.... SLPK.Q...E QKDKD..PPP .LVSLKSLFG
CRF01 AE T
           ..... MGEE..... QKDKE..HPP PSVSLKSLFG
CRF01 AE T
           ..... MGEETT.... SSLK.Q...E QKDKE..PPP PLISLKSLFG
CRF01 AE T
CRF01 AE T
           ..... MGEEITGEEI TSLPKQ...E QKDKE..HPP PLVSLKSLFG
CRF01_AE T
           ..... MGEEIT.... SFLK.Q...E QKDKE..HPP PSVSLKSLFG
           ..... MGEEIT.... SPPK.Q...E ARDQG..LYP PLASLKSLFG
CRF02 AG F
CRF02_AG_F
           ..... MGEEIT.... SPPK.Q...E PRDQG..LYP PLASLKSLFG
           ..... TREEITSS....PQQE.... PRDKG..LYP PLTSLKSLFG
CRF02_AG G
           ..... MGEEIP.... PSPQ.Q...E PRDKG..LYP PLTSLKSLFG
CRF02 AG N
           ..... IGEEIT.... SSQK.Q...E PGDKG..LYP PLASLKSLFG
CRF02 AG S
           ..... MGEEIT.... SSPK.Q...E PGDKG..LYP PLTSLKSLFG
CRF02_AG_S
           ..... MGEEIT.... PSLK.Q...E QKDRE..QHP PSISLKSLFG
CRF03 AB R
           ..... MGEEIT.... PSLK.Q...E QKDRG..QHP PSISLKSLFG
CRF03_AB_R
           ..... RKEETTS... S.LK.Q...E PRDKE..LYP .LTSLKSLFG
CRF04_cpx_
           ..... MKEETTS... S.PK.Q...E PRDKE..LYP .LTSLKSLFG
CRF04_cpx_
           ..... MKEETTS... S.PK.Q...E QRDKE..LYP .ITSLKSLFG
CRF04_cpx_
           ..... FGEEIAS... .SPKQE...Q KDEG...LYP PLASLKSLFG
CRF05_DF_B
CRF05_DF_B
           ..... FGEEITP... .SPKQE...Q KDEG...KYP PLASLKSLFG
           ..... FGEEIAP... S.PK.Q...E SKEKEEKGLY PLASLKSLFG
CRF06_cpx_
           ..... FGEETAP... S.PE.Q...K PKEKE...LY PLTSLRSLFG
CRF06_cpx_
           ..... FGEETAP... S.LK.Q...E PKEKEKE.LY PLASLKSLFG
CRF06_cpx_
           ..... FGEEIAP... S.PK.Q...E PKEKE...LY PLASLKSLFG
CRF06 cpx
CRF11 cpx
           ..... FGEEIAP... .SPK.Q...E PKEKEK.ELY PLTSLKSLFG
           ..... FGEETTP... .SPK.Q...E PKEK...ELY PITSLKSLFG
CRF11 cpx
           ..... FGEEITP... .SQKQEQK.. DKDK...ELY PLASLKSLFG
D CD 84ZR0
D CD ELI K
           ..... FGEEITP... SQKQE...Q KDK....ELY PLTSLKSLFG
           ..... FGEEITP... .SQKQE...Q KDK....ELY PLASLKSLFG
D CD NDK M
           ..... LGEEITP... .PQKQE...Q KDK....ELY PLTSLKSLFG
D UG 94UG1
F1 BE VI85
           .....FR... .EEITPSP.. ...KQE.... QKDGEL..YP PLASLKSLFG
           .....FG... .EETTPSP.. ...KQE.... QKDEGL..YP PLASLKSLFG
F1 BR 93BR
           .....IR... .EEVTPSP.. ...RQE.... QKEEGQ..YP PLASLKSLFG
F1 FI FIN9
F1 FR MP41
           .....FK... .EEITPSP.. ...KQE.... QKDEGQGLYP PLASLKSLFG
           .....FG... .EEIAPSP.. ...KQE.... QKDKEQ..VP PLISLKSLFG
F2 CM MP25
           .....FG... .EEINPSP.. ...RQE.... TKDKGQ..EP PLTSLKSLFG
F2KU BE VI
           ..... FGEEIAP... S.PK.Q...E QKEKE..LYP L.SSLKSLFG
G BE DRCBL
           ..... FGEEIAP... S.PK.Q...E PKEKE..LYP L.TSLKSLFG
G NG 92NG0
           ..... FGEEIAP... S.PK.Q...E MKEKE..LYP ...SLKSLFG
G SE SE616
           .....FG... .EEITPSP.. ...RQE.... LKEQE....P PLTSLRSLFG
H BE VI991
           .....FG... .EEMTSSP.. ...KQE.... LKDKE....P PFASLKSLFG
H BE VI997
H_CF_90CF0
           .....FG... .EEMTPSP.. ...KQEQ... LKDKE....P PLASLRSLFG
           .....FG... .EEIPSP.. ...KQE.... PKDKE...LY PLTSLRSLFG
J_SE_SE702
           .....LG... ..EEIPSP.. ...KQE.... PKDKE...LY PLTSLKSLFG
J_SE_SE788
           .....FG... .EKITPSL.. ...RQE.... MKDQEQ..GP PLTSLKSLFG
K_CD_EQTB1
           .....FG... .EEITPSP.. ...RQE.... TKDKEQ..SP PLTSLKSLFG
K CM MP535
           .....FQ... ..EEKSTQ.. GKEMQE...N QERTENSLYP PLTSLRSLFG
N_CM_YBF30
           .....LY PFASLKSLFG
O CM_ANT70
O_CM_MVP51
           ..... . EQENQSQ.....KGD.... QEE.....LY PFASLKSLFG
           O SN 99SE
           O_SN_99SE
           .....FG... .EETTPSP.. ...KQE.... PRDKESL.YP PLTSLKSLFG
U CD 83C
           551
00BW0762 1
           SDPLSQ
00BW0768_2
           SDPLSQ
00BW0874_2
           NDPLSQ
00BW1471 2
           SDPLSQ
00BW1616 2
           SDPLSQ
```

```
00BW1686_8 SDPLSQ
00BW1759 3
            SDPLSQ
00BW1773 2
            SDPLSQ
00BW1783 5
            SDPLSQ
00BW1795 6
            SDPLSQ
00BW1811_3
            SDPLSQ
00BW1859_5
            SDPLSQ
00BW1880_2
            NDPLSQ
00BW1921_1
            SDPLSQ
00BW2036_1
            SDPLSQ
00BW2063_6
            NDPLSQ
00BW2087_2
            SDPLSQ
00BW2127_2
            SDPLSQ
00BW2128_3
            SDPWSQ
00BW2276_7
            SDPLSQ
00BW3819_3
            SDPLSQ
00BW3842_8
            SDPLSQ
00BW3871_3
            SDPLSQ
            SDPLSQ
00BW3876_9
            SDPLSQ
00BW3886_8
00BW3891_6
            SDPLSQ
00BW3970_2
            SDPLSQ
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            SDPLSQ
 96BW01B21
            SDPLSQ
  96BW0407
            NDPLSQ
  96BW0502
            SGPLSQ
 96BW06_J4
            SDPLSQ
 96BW11 06
            SDPLSQ
  96BW1210
            NDPLSQ
 96BW15B03
            SDPLSO
 96BW16 26
            NDPLSQ
            SDPLSQ
 96BW17A09
 96BWMO1_5
            SDPLSQ
 96BWMO3_2
            SDPLSQ
98BWMC12 2
            NDPLSQ
98BWMC13_4
            SDPLSQ
98BWMC14_a
            NDPLSQ
98BWM014_1
98BWM018_d
            SDPLSQ
            SDPLSQ
98BWMO36_a
            SDPLSQ
98BWM037_d
            SDPLSQ
99BW3932<u>1</u>
            SDPLSQ
99BW4642_4
            SDPLSQ
99BW4745_8
            SDPLSQ
99BW4754_7
            NDPLSQ
99BWMC16_8
            GDPLSQ
A2_CD_97CD
            NDLLSQ
A2_CY_94CY
           NDPLLQ
A2D 97KR NDPLLQ
A2G_CD_97C
            . . . . . .
A_BY_97BL0 NDPLSQ
A_KE_Q23_A
            NDLLSQ
A SE SE659
A SE SE725
            . . . . . .
A SE SE753 NDLLSQ
A SE SE853
A SE SE889
A SE UGSE8 NDLLSQ
A_UG_92UG0 NDLLSQ
A_UG_U455_
            NDPLSQ
```

```
SDPLSQ
AC_IN_2130
AC_RW_92RW
            NDPLSQ
AC SE SE94
             . . . . . .
ACD SE SE8
            NDP...
ACG BE VI1
            NDP...
AD SE SE69
            NDP...
AD SE SE71
             . . . . . .
ADHK NO 97
            NDPLSQ
ADK_CD_MAL
            NDQLSQ
AG BE VI11
            NDP...
AG NG 92NG
            NDP...
AGHU GA VI
            SDP...
AGU_CD_Z32
            SDP...
AJ BW BW21
            SDP...
B_AU_VH_AF
            NDPSSQ
B_CN_RL42_
            NDPSSQ
B_DE_D31_U
            NDPSSQ
B_DE_HAN_U
            SDPSSQ
B_FR_HXB2_
            NDPSSQ
B_GA_OYI__
            NDPSSQ
B_GB_CAM1_
            NDPSSQ
B_GB_GB8_A
            NDPSSQ
B_GB_MANC_
            NDPSSQ
B_KR_WK_AF
            NDPSSQ
B_NL_3202A
            NDPSSQ
B_TW_TWCYS
            NDPSSQ
B US BC LO
            NDPSSQ
B US DH123
            NDP...
B US JRCSF
            NDPSSQ
B US MNCG
            NDPLSQ
B US P896
            NDPSSQ
B US RF M1
            NDPSSQ
B US SF2 K
            NDPSSQ
B US WEAU1
            NDPSSQ
B_US_WR27_
            NDPSSQ
B US YU2 M
            SDPSSQ
BF1_BR_93B
            NDPSSQ
C_BR_92BR0
            SDPLST
C_BW_96BW0
            SDPLSQ
C_BW_96BW1
            SDPLSQ
C_BW_96BW1
            NDPLSQ
C_BW_96BW1
            SDPLSQ
C ET ETH22
            NDHLLQ
C_IN_93IN1
            SDLLSQ
C_IN_93IN9
            SDPLSQ
C_IN_93IN9
            SDPLSQ
C_IN_94IN1
            SDPLSQ
C_IN_95IN2
            SDPLSQ
CRF01_AE_C
            NDPLSQ
            NDPLSQ
CRF01_AE_C
CRF01_AE_C
            NDPLSQ
CRF01_AE_T
            NDPSSQ
CRF01_AE_T
            NDPLSQ
CRF01_AE_T
            NDPLSQ
CRF01_AE_T
            NDPLSQ
CRF01_AE_T
            NDPLSQ
CRF01_AE_T
            NDPLSQ
CRF02_AG_F
            NDP...
CRF02 AG_F
            NDP...
CRF02 AG G
            NDP...
```

```
CRF02_AG_N
             NDP...
CRF02 AG S
             NDP...
CRF02_AG_S
             NDPYSQ
CRF03_AB_R
             DDPLSQ
CRF03_AB_R
             NDPLSQ
CRF04_cpx_
             SDPLSQ
CRF04_cpx_
             NHPLSQ
CRF04_cpx_
CRF05_DF_B
             SDPLSR
             NDPLSQ
CRF05_DF_B
             NDPLSQ
CRF06_cpx_
             SDP...
CRF06_cpx_
             NDP...
CRF06_cpx_
             NDP...
CRF06_cpx_
             SDP...
CRF11_cpx_
             SDP...
CRF11_cpx_
             SDPLSQ
D_CD_84ZR0
             NDPLSQ
D_CD_ELI_K
             NDPLSQ
D_CD_NDK_M
             NDPSSQ
D_UG_94UG1
             NDPLSQ
F1_BE_VI85
             \mathtt{NDP}\dots
             NDP...
F1_BR_93BR
             NDP...
F1_FI_FIN9
F1 FR MP41
             SDP...
F2 CM MP25
             SDQ...
F2KU BE VI
             SDPLLQ
G BE DRCBL
             NDQ...
G_NG_92NG0
             SDP...
G_SE_SE616
             SDP...
H BE VI991
             NDQ...
H_BE_VI997
             NDPLSQ
H_CF_90CF0
             SDPLLQ
J_SE_SE702
             SDPLSQ
J_SE_SE788
             SDPLSQ
K CD EQTB1
             SDPLSQ
K CM MP535
             NDPLSQ
N_CM_YBF30
             NDPSSQ
O_CM_ANT70
             TDQ...
O CM_MVP51
             TDQ...
O_SN_99SE_
             TDQ...
O_SN_99SE_
             TDQ...
U_CD___83C
             SDPSLQ
```

Table 12. HIV Env Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

Name:	00BW0762_1	SEQ ID N	10: 469	Len:	962	Check:	4645	Weight:	1.00
Name:	00BW0768_2	SEQ ID N	JO: 470	Len:	962	Check:	9565	Weight:	1.00
Name:	00BW0874_2	SEQ ID N	10: 471	Len:	962	Check:	7745	Weight:	1.00
Name:	00BW1471_2	SEQ ID N	IO: 472	Len:	962	Check:	9593	Weight:	1.00
Name:	00BW1616 2	SEQ ID N	IO: 473	Len:	962	Check:	792	Weight:	1.00
Name:	00BW1686 8	SEQ ID N	IO: 474	Len:	962	Check:	3744	Weight:	1.00
Name:	00BW1759 3	SEQ ID N	IO: 475	Len:	962	Check:	9808	Weight:	1.00
Name:	00BW1773 2	SEQ ID N	10: 476	Len:	962	Check:	3500	Weight:	1.00
Name:	00BW1783 5	SEQ ID N	JO: 477	Len:	962	Check:	9684	Weight:	1.00
Name:	00BW1795 6	SEQ ID N	JO: 478	Len:	962	Check:	8410	Weight:	1.00
Name:	00BW1811 3	SEQ ID N	IO: 479	Len:	962	Check:	2068	Weight:	1.00
Name:	00BW1859 5	SEQ ID N	IO: 480	Len:	962	Check:	5692	Weight:	1.00
Name:	00BW1880 2		IO: 481	Len:	962	Check:	1901	Weight:	1.00
Name:	00BW1921 1		TO: 482	Len:	962	Check:	5923	Weight:	1.00
Name:	_		IO: 483	Len:	962	Check:		Weight:	1.00
Name:	00BW2063 6		IO: 484	Len:	962	Check:	4853	Weight:	1.00
Name:	00BW2087 2		IO: 485	Len:	962	Check:	2085	Weight:	1.00
Name:	00BW2127 2		IO: 486	Len:	962	Check:		Weight:	1.00
Name:	00BW2128 3		IO: 487	Len:	962	Check:		Weight:	1.00
Name:	00BW2276 7		10: 488	Len:	962	Check:		Weight:	1.00
Name:	00BW3819 3		IO: 489	Len:	962	Check:		Weight:	1.00
Name:	00BW3842 8		io: 490	Len:	962	Check:		Weight:	1.00
Name:	00BW3871 3		IO: 491	Len:	962	Check:	7069	Weight:	1.00
Name:	00BW3876 9		IO: 492	Len:	962	Check:		Weight:	1.00
Name:	00BW3886 8		io: 493	Len:	962	Check:		Weight:	1.00
Name:	00BW3891 6		IO: 494	Len:	962	Check:		Weight:	1.00
Name:	00BW3970 2		io: 495	Len:	962	Check:		Weight:	1.00
Name:	00BW5031 1		10: 496	Len:	962	Check:		Weight:	1.00
Name:	96BW01B21		IO: 497	Len:	962	Check:		Weight:	1.00
Name:	96BW0407		TO: 498	Len:	962	Check:		Weight:	1.00
Name:	96BW0502		io: 499	Len:	962	Check:		Weight:	1.00
Name:	96BW06 J4		io: 500	Len:	962	Check:		Weight:	1.00
Name:	96BW11 06		io: 501	Len:	962	Check:		Weight:	1.00
Name:	96BW1210		iO: 502	Len:	962	Check:		Weight:	1.00
Name:	96BW15B03		IO: 503	Len:	962	Check:		Weight:	1.00
Name:	96BW16 26		IO: 504	Len:	962	Check:		Weight:	1.00
Name:	96BW17A09	~	IO: 505	Len:	962	Check:		Weight:	1.00
Name:	96BWM01 5		IO: 506	Len:	962	Check:	9487	Weight:	1.00
Name:	96BWMO3 2		10: 507	Len:	962	Check:		Weight:	1.00
Name:	98BWMC12 2		10: 508	Len:	962	Check:		Weight:	1.00
Name:	98BWMC13 4		TO: 509	Len:	962	Check:		Weight:	1.00
	98BWMC14 a				962	Check:		Weight:	1.00
	98BWM014 1			Len:	962	Check:		Weight:	1.00
	98BWM018 d			Len:		Check:		Weight:	1.00
	98BWMO36_a			Len:	962	Check:		Weight:	1.00
	98BWM037 d			Len:	962	Check:		Weight:	1.00
	99BW3932_1			Len:	962	Check:		Weight:	1.00
	99BW4642 4			Len:		Check:		Weight:	1.00
	99BW4745_8			Len:		Check:		Weight:	1.00
Name:	_			Len:	962	Check:		Weight:	1.00
	99BWMC16 8			Len:	962	Check:		Weight:	1.00
	A2_CD_97CD			Len:	962	Check:		Weight:	1.00
	A2 CY 94CY			Len:		Check:		Weight:	1.00
Name:				Len:		Check:		Weight:	1.00
	A2G CD 97C			Len:		Check:		Weight:	1.00
	A BY 97BL0			Len:		Check:		Weight:	1.00
		<u> </u>						3	

```
Name: A_KE_Q23_A SEQ ID NO: 525 Len: 962
                                            Check: 1190
                                                          Weight:
                                                                     1.00
Name: A SE SE659 SEQ ID NO: 526 Len: 962
                                            Check: 6674
                                                          Weight:
                                                                     1.00
Name: A SE SE725 SEQ ID NO:
                             527 Len: 962
                                            Check: 4925
                                                          Weight:
                                                                     1.00
                                                                     1.00
Name: A SE SE753 SEQ ID NO: 528 Len: 962
                                            Check: 2482
                                                          Weight:
Name: A_SE_SE853 SEQ ID NO: 529 Len: 962
                                            Check: 1860
                                                          Weight:
                                                                     1.00
                                            Check: 2102
                                                          Weight:
                                                                     1.00 ~
Name: A SE SE889 SEQ ID NO:
                             530 Len: 962
                                                          Weight:
                                                                     1.00
Name: A_SE_UGSE8 SEQ ID NO:
                             531 Len: 962
                                            Check: 5063
Name: A UG 92UG0 SEQ ID NO:
                             532 Len: 962
                                            Check: 6685
                                                          Weight:
                                                                     1.00
Name: A_UG_U455_ SEQ ID NO: Name: AC_IN_2130 SEQ ID NO:
                              533 Len: 962
                                            Check: 8657
                                                          Weight:
                                                                     1.00
                                            Check: 7784
                              534 Len: 962
                                                          Weight:
                                                                     1.00
                                                          Weight:
Name: AC RW 92RW SEQ ID NO:
                                            Check: 4676
                              535 Len: 962
                                                                     1.00
Name: AC SE SE94 SEQ ID NO:
                             536 Len: 962
                                            Check: 2949
                                                          Weight:
                                                                     1.00
Name: ACD SE SE8 SEQ ID NO:
                                            Check: 1464
                             537 Len: 962
                                                          Weight:
                                                                     1.00
Name: ACG BE VI1 SEQ ID NO: 538 Len: 962
                                            Check: 2980
                                                          Weight:
                                                                     1.00
Name: AD_SE_SE69 SEQ ID NO: 539 Len: 962
                                            Check: 8959
                                                          Weight:
                                                                     1.00
Name: AD_SE_SE71 SEQ ID NO:
                                            Check: 7056
                             540 Len: 962
                                                          Weight:
                                                                     1.00
Name: ADHK_NO_97 SEQ ID NO:
                             541 Len: 962
                                            Check: 487
                                                          Weight:
                                                                     1.00
Name: ADK_CD_MAL SEQ ID NO:
                             542 Len: 962
                                            Check: 2555
                                                          Weight:
                                                                     1.00
Name: AG_BE_VI11 SEQ ID NO: 543 Len: 962
                                            Check: 6342
                                                          Weight:
                                                                     1.00
Name: AG_NG_92NG <u>SEQ ID NO: 544</u> Len: 962
                                            Check: 1272
                                                          Weight:
                                                                     1.00
Name: AGHU_GA_VI SEQ ID NO: 545 Len: 962
                                            Check: 1974
                                                          Weight:
                                                                     1.00
Name: AGU_CD_Z32 SEQ ID NO: 546 Len: 962
                                            Check: 4356
                                                          Weight:
                                                                     1.00
Name: AJ_BW_BW21 SEQ ID NO: 547 Len: 962
                                                          Weight:
                                            Check: 9995
                                                                     1.00
Name: B_AU_VH_AF_SEQ_ID_NO: 548 Len: 962
                                                                     1.00
                                            Check: 5833
                                                          Weight:
Name: B_CN_RL42_ SEQ_ID_NO: 549 Len: 962
                                            Check: 4092
                                                          Weight:
                                                                     1.00
                                            Check: 5486
Name: B DE D31 U SEQ ID NO: 550 Len: 962
                                                          Weight:
                                                                     1.00
Name: B DE HAN U SEQ ID NO: 551 Len: 962
                                            Check: 3480
                                                          Weight:
                                                                     1.00
Name: B_FR_HXB2_ SEQ ID NO: 552 Len: 962
                                            Check: 6939
                                                          Weight:
                                                                     1.00
                                            Check: 9780
                                                                     1.00
Name: B_GA_OYI__ SEQ ID NO: 553 Len: 962
                                                          Weight:
Name: B GB CAM1 SEQ ID NO: 554 Len: 962
                                            Check: 9716
                                                          Weight:
                                                                     1.00
Name: B GB GB8 C SEQ ID NO: 555 Len: 962
                                            Check: 4180
                                                          Weight:
                                                                     1.00
Name: B GB MANC SEQ ID NO: 556 Len: 962
                                            Check: 9762
                                                          Weight:
                                                                     1.00
Name: B KR WK AF SEQ ID NO: 557 Len: 962
                                            Check: 6641
                                                          Weight:
                                                                     1.00
Name: B NL 3202A SEQ ID NO: 558 Len: 962
                                            Check: 7168
                                                          Weight:
                                                                     1.00
Name: B TW TWCYS SEQ ID NO: 559 Len: 962
                                            Check: 3591
                                                          Weight:
                                                                     1.00
Name: B US BC LO SEQ ID NO: 560 Len: 962
                                            Check: 7266
                                                          Weight:
                                                                     1.00
                                            Check: 6905
                                                          Weight:
Name: B_US_DH123 SEQ ID NO: 561 Len: 962
                                                                     1.00
Name: B US JRCSF SEQ ID
                         NO: 562 Len: 962
                                            Check: 9381
                                                          Weight:
                                                                     1.00
Name: B_US_MNCG_ SEQ ID
                         NO:
                             563 Len: 962
                                            Check: 9951
                                                          Weight:
                                                                     1.00
Name: B_US_P896_ SEQ_ID
Name: B_US_RF_M1 SEQ_ID
                         NO:
                             564 Len: 962
                                            Check: 5855
                                                          Weight:
                                                                     1.00
                                            Check: 6075
                         NO: 565 Len: 962
                                                          Weight:
                                                                     1.00
Name: B_US_SF2_K SEQ ID
                                            Check: 1434
                         NO: 566 Len: 962
                                                          Weight:
                                                                     1.00
Name: B US WEAU1 SEQ ID
                                            Check: 5451
                                                          Weight:
                                                                     1.00
                         NO:
                             567 Len: 962
Name: B_US_WR27_ SEQ ID
                         NO:
                             568 Len: 962
                                            Check: 4262
                                                          Weight:
                                                                     1.00
Name: B US YU2 M SEQ ID
                         NO:
                             569 Len: 962
                                            Check: 5841
                                                          Weight:
                                                                     1.00
Name: BF1_BR_93B SEQ ID
                         NO:
                             570 Len: 962
                                            Check: 5506
                                                          Weight:
                                                                     1.00
Name: C_BR_92BR0 SEQ ID
                             571 Len: 962
                                            Check: 8769
                                                          Weight:
                                                                     1.00
                         NO:
Name: C_BW_96BW0 SEQ ID
                         NO:
                             572 Len: 962
                                            Check: 6197
                                                          Weight:
                                                                     1.00
Name: C_BW_96BW1 SEQ ID NO: 573 Len: 962
                                            Check: 8144
                                                          Weight:
                                                                     1.00
                                            Check: 1160
                                                          Weight:
                                                                     1.00
Name: C_BW_96BW1 SEQ_ID_NO: 574 Len: 962
                                                          Weight:
Name: C_BW_96BW1 SEQ ID NO: 575 Len: 962
                                            Check: 2736
                                                                     1.00
                                                          Weight:
Name: C_ET_ETH22 SEQ ID NO: 576 Len: 962
                                            Check: 8219
                                                                     1.00
Name: C_IN_93IN1 SEQ ID NO: 577 Len: 962
                                            Check: 4068
                                                          Weight:
                                                                     1.00
Name: C_IN_93IN9 <u>SEQ ID NO: 578</u> Len: 962
                                            Check: 3674
                                                          Weight:
                                                                     1.00
Name: C_IN_93IN9 SEQ ID NO: 579 Len: 962
                                            Check: 1581
                                                          Weight:
                                                                     1.00
                                            Check: 9352
                                                          Weight:
                                                                     1.00
Name: C_IN_94IN1 <u>SEQ ID NO: 580</u> Len: 962
                                                          Weight:
                                                                     1.00
                                            Check: 6988
Name: C_IN_95IN2 SEQ ID NO: 581 Len: 962
                                                          Weight:
                                            Check: 8684
                                                                     1.00
Name: CRF01_AE_C SEQ ID NO: 582 Len: 962
                                                          Weight:
                                                                     1.00
Name: CRF01 AE C SEQ ID NO: 583 Len: 962
                                            Check: 3342
Name: CRF01_AE_C SEQ ID NO: 584 Len: 962
                                            Check: 5017
                                                          Weight:
                                                                     1.00
```

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Name: CRF01 AE T SEQ ID NO: 585 Len: 962
                                             Check: 9124
                                                           Weight:
                                                                      1.00
                                                           Weight:
                                                                      1.00
Name: CRF01 AE T SEQ ID NO: 586 Len: 962
                                             Check: 2718
                                                           Weight:
                                             Check: 2104
                                                                      1.00
Name: CRF01 AE T SEQ ID NO: 587 Len: 962
                                                           Weight:
                                                                      1.00
                                             Check: 8495
Name: CRF01 AE T SEQ ID NO: 588 Len: 962
                                             Check: 4076
                                                           Weight:
                                                                      1.00
Name: CRF01 AE T SEQ ID
                          NO:
                              589 Len: 962
                                                                      1.00
Name: CRF01 AE T SEQ ID
                                              Check: 948
                                                           Weight:
                          NO:
                              590 Len: 962
                                             Check: 9298
                                                           Weight:
                                                                      1.00
Name: CRF02 AG F SEQ ID
                          NO:
                              591 Len: 962
                                                           Weight:
Name: CRF02 AG F SEQ ID NO:
                              592 Len: 962
                                              Check: 9278
Name: CRF02 AG G SEQ ID NO:
                              593 Len: 962
                                              Check: 4373
                                                            Weight:
Name: CRF02 AG N SEQ
                       ID NO:
                              594 Len: 962
                                             Check: 8955
                                                            Weight:
                                                                      1.00
Name: CRF02 AG S SEQ
                                             Check: 252
                                                            Weight:
                                                                      1.00
                       ID NO:
                              595 Len: 962
Name: CRF02 AG S SEQ
                                                            Weight:
                                                                      1.00
                              596 Len: 962
                                             Check: 5147
                       ID
                          NO:
                                                           Weight:
                                                                      1.00
Name: CRF03 AB R SEQ
                              597 Len: 962
                                             Check: 2239
                       ID
                          NO:
                                             Check: 2671
                                                           Weight:
                                                                      1.00
Name: CRF03_AB_R SEQ
                              598 Len: 962
                       ID NO:
                                                           Weight:
                              599 Len: 962
                                             Check: 4892
                                                                      1.00
Name: CRF04_cpx_ <u>SEQ</u>
                       ID NO:
                                             Check: 8070
                                                           Weight:
                                                                      1.00
Name: CRF04_cpx_ <u>SEQ</u>
                       ID NO:
                              600 Len: 962
Name: CRF04_cpx_ <u>SEQ</u>
                       ID NO:
                              601 Len: 962
                                             Check: 5453
                                                           Weight:
                                                                      1.00
Name: CRF05_DF_B SEQ
                       ID
                          NO: 602 Len: 962
                                             Check: 174
                                                            Weight:
                                                                      1.00
                              603 Len: 962
                                              Check: 2694
                                                            Weight:
                                                                      1.00
Name: CRF05_DF_B SEQ
                       ID NO:
                                              Check: 7351
                                                            Weight:
                                                                      1.00
Name: CRF06_cpx_ SEQ
                       ID NO: 604 Len: 962
Name: CRF06_cpx_ SEQ
                       ID
                          NO: 605 Len: 962
                                              Check: 5073
                                                            Weight:
                                                                      1.00
Name: CRF06_cpx_ SEQ
                       ID
                          NO: 606 Len: 962
                                              Check: 661
                                                            Weight:
                                                                      1.00
                                                            Weight:
Name: CRF06_cpx_ <u>SEQ</u>
                       ID
                          NO: 607 Len: 962
                                              Check: 8440
                                                                      1.00
Name: CRF11_cpx_ SEQ ID
                                              Check: 2217
                                                            Weight:
                                                                      1.00
                          NO: 608 Len: 962
                                              Check: 8216
Name: CRF11_cpx_ <u>SEQ</u>
                      ID
                          NO: 609 Len: 962
                                                            Weight:
                                                                      1.00
                          NO: 610 Len: 962
                                                            Weight:
                                                                      1.00
Name: D CD 84ZR0 SEQ ID
                                              Check: 4843
                                                            Weight:
                                                                      1.00
                                             Check: 8403
Name: D CD ELI K SEQ ID
                          NO: 611 Len: 962
                                              Check: 5813
                                                            Weight:
                                                                      1.00
                          NO: 612 Len: 962
Name: D CD NDK M SEQ ID
                                                                      1.00
                                             Check: 9407
                                                            Weight:
Name: D UG 94UG1 SEQ ID
                          NO:
                              613 Len: 962
                                              Check: 2982
                                                            Weight:
                                                                      1.00
Name: F1 BE VI85 SEQ ID
                          NO:
                              614 Len: 962
                                                                      1.00
Name: F1 BR 93BR SEO ID
                              615 Len: 962
                                              Check: 8919
                                                            Weight:
                          NO:
Name: F1 FI FIN9 SEQ ID
                              616 Len: 962
                                              Check: 6761
                                                            Weight:
                                                                      1.00
                          NO:
Name: F1 FR MP41 SEQ ID
                          NO:
                              617
                                  Len: 962
                                              Check: 478
                                                            Weight:
                                                                      1.00
                                              Check: 9292
                                                            Weight:
                                                                      1.00
Name: F2 CM MP25 SEQ ID
                          NO:
                              618 Len: 962
                          NO:
                                                            Weight:
                                                                      1.00
Name: F2KU BE VI SEQ
                       ID
                              619
                                  Len: 962
                                              Check: 567
                                                                      1.00
Name: G BE DRCBL SEQ ID
                              620 Len: 962
                                              Check: 6261
                                                            Weight:
                          NO:
                               621 Len: 962
Name: G_NG_92NG0 SEQ ID
                                              Check: 4508
                                                            Weight:
                                                                      1.00
                          NO:
                                              Check: 6733
                                                            Weight:
                                                                      1.00
Name: G SE_SE616 SEQ ID
                          NO:
                              622 Len: 962
Name: H BE VI991 SEQ ID
                          NO:
                              623 Len: 962
                                              Check: 7498
                                                            Weight:
                                                                      1.00
Name: H_BE_VI997 SEQ ID
                                              Check: 8345
                                                            Weight:
                                                                      1.00
                          NO:
                               624
                                  Len: 962
Name: H CF 90CF0 SEQ
                                              Check: 2490
                                                            Weight:
                                                                      1.00
                       ID
                          NO:
                              625
                                  Len: 962
                                              Check: 4446
                                                            Weight:
                                                                      1.00
Name: J SE SE702 SEQ
                                  Len: 962
                       ID
                          NO:
                              626
Name: J_SE_SE788 SEQ
                                              Check: 1662
                                                            Weight:
                                                                       1.00
                       ID
                          NO: 627
                                   Len: 962
                                              Check: 7406
                                                            Weight:
                                                                       1.00
Name: K CD EQTB1 SEQ ID
                          NO: 628
                                   Len: 962
                                                                       1.00
Name: K_CM_MP535 SEQ
                       ID
                          NO: 629
                                   Len: 962
                                              Check: 512
                                                            Weight:
Name: N_CM_YBF30 SEQ ID
                                              Check: 1733
                                                            Weight:
                                                                       1.00
                          NO: 630
                                  Len: 962
Name: O_CM_ANT70 SEQ ID NO: 631 Len: 962
                                              Check: 75
                                                            Weight:
                                                                       1.00
                                                                       1.00
Name: O_CM_MVP51 SEQ ID NO: 632
                                  Len: 962
                                              Check: 3290
                                                            Weight:
Name: O_SN_99SE_ <u>SEQ ID NO: 633</u> Len: 962
                                                                       1.00
                                              Check: 6963
                                                            Weight:
Name: O_SN_99SE_ <u>SEQ ID NO: 634</u> Len: 962
Name: U_CD___83C <u>SEQ ID NO: 635</u> Len: 962
                                              Check: 6278
                                                            Weight:
                                                                       1.00
                                              Check: 9044
                                                            Weight:
                                                                       1.00
                                                                              50
SEQ ID NO
                      ....MRVMGI MRNC.QQWWI WV.ILGFWML MVCN.VIGNL WVTVYYGVPV
         00BW0762 1
469
                       ....MRVREI LRNC.QQWWT WG.SLGFWMV MIYS.VVGEL WVTVYYGVPV
470
         00BW0768 2
                       ....MRAMGT QRNC.RQWWI WG.ILGFWML MTCS.GVG.E MVTVYYGVPV
         00BW0874 2
471
                       ....MRVMGI LRSC.QQWWI WG.ILGFWML MICS.VLGNL WVTVYYGVPV
472
         00BW1471 2
                       ....MRVMGI QRNC.QRWWI WG.ILGFWMI Y..N.VVGNL WVTVYYGVPV
473
         00BW1616 2
                      ....MRVKGI QRNW.PQWWI WG.SLGFWML MFYS.VMGNL WVTVYYGVPV
         00BW1686 8
<u>47</u>4
```

```
....MRVRGI PRNW.QQWWI WG.ILGFCMI ITCK.VVGNL WVTVYYGVPV
475
         00BW1759 3
                     ....MRVREI LRSY.QHWWM WS.ILGLWIL IISN.VVGNL WVTVYYGVPV
476
         00BW1773 2
                     ....MRVMGI KRNC.PPWWI WG.ILGFWML MICN.VMGNL WVTVYYGVPV
         00BW1783 5
477
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98BWMC12_2
98BWMC13_4
98BWMC13_4
98BWMC14_a
98 98BWMO18_d WREAKATLFC ASNAKAYEKE VHNVWATHAC VPTDPNPQEM VLENVTENFN 98BWMO36_a WKEAKATLFC ASDAKAYDKE VHNVWATHAC VPTDPDPQEI VLENVTESFN 98BWMO37_d WKEAKTTLFC ASDAKAYDKE VHNVWATHAC VPTDPNPQEM VLENVTENFN 99BW3932_1 WKEAKATLFC ASDAKAYEKE VHNVWATHAC VPTDPNPQKL VLGNVTENFN 99BW4642_4 WKEAKTTLFC ASDAKAYDKE VHNVWATHAC VPTDPNPQEI VLENVTENFN 99BW4745_8 WREAKTTLFC ASDAKAYEKE VHNVWATHAC VPTDPNPQEL VLKNVTENFN 99BW4754_7 WREAKTTLFC ASDAKAYDKE VHNVWATHAC VPTDPNPQEI VLENVTENFN 99BWMC16_8 WREAKATLFC ASDAKAYERE VHNVWATHAC VPTDPDPQEI ALENVTENFN A2_CD_97CD WRDADTTLFC ASDAKAYATE KHNVWATHAC VPTDPNPQEV NLANVTEDFN A2_CY_94CY WKDADTILFC ASDAKAYDTE VHNVWATHAC VPTDPNPQEI NLENVTENFN A2D___97KR WRDAETTLFC ASDAKAYDTE AHNVWATHAC VPTDPNPQEI NLENVTENFN A2G_CD_97C WEDANTPLFC ASDAKSYSTE RHNVWATHAC VPTDPNPQEM ILENVTESFN A_BY_97BL0 XXDAATTLFC ASDAKAXDKE VHNVWATHAC VPTDPDPQEI ILGNVTEKFD A KE Q23 A WRDADTTLFC ASDAKAYETE KHNVWATHAC VPTDPNPQEI HLDNVTEKFN A SE SE659 WKDAETTLFC ASDAKAYDPE VHNVWATHAC VPTDPNPQEM HLENVTEESN A_SE_SE725 WKDAETTLFC ASDAQAYKTE MHNVWATHAC VPTDPNPQEL HLKNVTEEFN

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C ET ETH22
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CRF01 AE T
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CRF06_cpx_
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O SN 99SE
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K CM MP535
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N CM YBF30
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O CM ANT70
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O CM MVP51
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U CD 83C
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00BW1686 8		PLEE			
00BW1759 3		PLEGE			
00BW1773 2	HALFYRLDIV	QLD	N	ss	YRLI
00BW1783 5		PLEGNNS			
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96BW11 06		PLNNKNE			
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96BWMO3 2		PLDGNNE			
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A2G_CD_97C		QINKDNN		.T	
A_BY_97BL0	NGT EADT DIA	STSNNDSX PINEN			
A_KE_Q23_A A SE SE659	TOULIANDIA TOULIANDIA	QMNEN	PCMCGMCGA	NE.	YRIT
A_SE_SE659 A SE SE725		QINDN		SE	YRLT
H_0E_0E/40	TOULTKINTA	ATMDM	· CHMCHIE	ош	

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A_SE_SE853				TQ	
A SE SE889				.L	
A SE UGSE8	YSLFYKLDIV	KINKNKSFRG	. KNSSGNSSS	DR	YRLI
A UG 92UG0	YSLFYKLDVV	QINNG	NNSS	NL	YRLI
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AC RW 92RW				NQ	
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ACD SE SE8				SQ	
ACG BE VI1				GK	
AD SE SE69				SQ	
AD SE SE71	VGI.EAKI'DAM	OTNENO	VNCCMNCN	KE	VRIT
ADHK NO 97				TQ	
ADK CD MAL				S	
	INITENDEDIA	OIDDON			CCVMT.T
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AGHU_GA_VI				SE	
AGU_CD_Z32					
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B_DE_D31_U				TS	
B_DE_HAN_U				TS	
B_FR_HXB2_				TS	
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B GB GB8 C	YALLYKLDIV	SIGSD	N	TS	YILT
B GB MANC	YALFYKLDVV	PIEKK	N	TS	FRLI
B KR WK AF	YALFYKLDII	PIDN		TS	YALR
B NL 3202A				TS	
B TW TWCYS				TS	
B US BC LO				TK	
B US DH123				TS	
B US JRCSF	ANT'EAKI'DAA	PTD	NKNN	TK	YRLI
B US MNCG	ANTI'AKI'DIA	SIDND	S	TS	YRLI
B US P896	VALENDI.D\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	DIE	NTNN	TK	YRLT
B US RF M1				GN	
B_US_RF_MI B US SF2 K				TN	
B_US_WEAU1				TS	
B_US_WR27_				AS	
B_US_YU2_M					
BF1_BR_93B				RE	
C_BR_92BR0				GD	
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C_ET_ETH22		PLN		TD	
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C IN 93IN9	YALFYRLDIV	QLNSDD.	KKNSS	EY	YRLI
C IN 93IN9	HALFYRLDLV	PLDNENKSS.		KT	
C IN 94IN1	YALFYKLDIV	PISETS.	NQS		RLI
C IN 95IN2		PLDNEEQEN.	DSNSS	GY	YRLI
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CRF03 AB R		QIDND			
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CRF05_DF_B	HALFYRLDIV	PISSDD	ssn	ss	YRLI
CRF05_DF_B		SINS			
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D_CD_ELI_K	YALFYRLDIV	PIDNDSS	TNS	TN	YRLI
D_CD_NDK_M		PIDNNNR			
D UG 94UG1		KINDNDS			
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F1_FI_FIN9		PISNNN.			
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F2_CM_MP25	YALFYKLDVV	QINNS		NTS	YRLI
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G BE DRCBL		PINEMNNENN			
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00BW1811_3	IVCIRPUNN.	.TRKSIRIG.	. PGOTFYATG	DIIGN	IREAHCNITR
00BW1839_3 00BW1880 2	IVCTRPNNN.	.TKKSIRIG.	. PGQTFYATG	DIIGD	IROAHCNISE
00BW1880_2 00BW1921 1	IECTRPNNN.	.TRKSHRIG.	. PGQTFYATG	DIIGN	TROAHCNVSA
00BW1921_1 00BW2036 1	IECIRPNNN.	.TRKSIRIG.	. PGQVFYATG	DIIGD	IREAHCNITE
00BW2030_1 00BW2063 6	IVCTRPGNN.	.TRKSTRIG.	. PGQTFYATG	EVIGD	IREAHCNISE
00BW2083_0	IVCTRPNNN.	.TRKSIRIG.	. PGOAFYATD	AIIGD	IRQAHCNISR
00BW2007_2	IVCTRPNNN.	.TRTSIRIG.	. PGHSFFATN	GIIGD	IROAHCSISK
00BW2127_2	INCTRPNNN.	.TRKSIRIG.	. PGOAFYATG	DIIGD	IROAHCNISK
00BW2126_3	IVCVRPNNN.	.TRKSVRIG.	. PGOTFFAT.	NIIGD	IREAHCNISE
00BW3819 3	IKCTRPNNN.	.TRRSVRIG.	. PGOAFYTN.	DIIGD	IRLAHCNISK
00BW3842 8	IVCTRPNNN.	.TRKSIRIG.	. PGOTFYAAG	DIIGN	IROAHCNISE
00BW3871 3	ITCTRPNNN.	.TRESIRIG.	. PGQTFYATG	DIIGD	IRKAYCNISI
00BW3876 9	IVCTRPNNN.	.IRKSVRIG.	. PGOAFYATG	DIIGD	IREAYCNING
00BW3886 8	IVCVRPNNN.	.TRKSIRIG.	. PGOTFYATG	EIIGN	IRQAYCSISG
00BW3891 6	IECTRPNNN.	.TRRSIRIG.	. PGQTFYATG	EIIGD	IRQAYCTINE
00BW3970 2	IECIRPNNN.	.TRKSIRIG.	. PGQTFYATN	GMIGD	IRQAHCNISG
00BW5031 1	IECRRPNNN.	.TGKSVRIG.	. PGQTFFATG	GIIGE	IRRAHCDING
96BW01B21	INCTRPNNN.	.TRKSIRIG.	. PGQTFYAAG	EIIGK	IRLAYCNISE
96BW0407	IECTGPNNN.	.TRKSMRIG.	. PGQTFYATG	EIVGD	IRQAHCNISE
96BW0502	IVCVRPNNN.	.TRKSVRIG.	. PGQTFYATG	EIIGD	IRQAYCIINK
96BW06_J4	IVCTRPNNN.	.TRKSIRIG.	.PGQTFYAT.	DIIGD	IRQAYCNVSK
96BW11_06	IVCIRPNNN.	.TRKSVRIG.	. PGQTFYATE	AIIGN	IREAHCNISE
96BW1210	IVCTRPNNN.	.TRKSIRIG.	. PGQTFYATG	DIIGD	IRQAHCNISK
96BW15B03	IVCTRPNNN.	.TRKGIRIG.	. PGQTFYATE	NIIGD	IRQAHCNISA
96BW16_26	IVCIRPNNN.	.TRKSIRIG.	. PGQTFFATG	DIIGD	IRQAHCIING
96BW17A09	IVCTRPNNN.	.TRKSTRIG.	. RGQTFYAMG	RIIGD	IRQAHCNISG
96BWM01_5	IECTRPGNN.	.TRRSVRIG.	. PGQAFYATG	DIIGD	IRAAHCNISE
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98BWMC12_2	IVCTRPNNN.	.TRKSMRIG.	. PGQIFYATG	EIIGN	
98BWMC13_4	IECTRPGNN.	.TRKSMRIG.		DIIGD	IROAHCNISE
98BWMC14_a 98BWMO14 1	IVCTRPNNN. IVCTRPGNN.	.TRTSIRIG.		DIIGD	IRQAHCNISE
98BWM014_1	ILCVRPSNN.	.TRKSVRIG.		DIIGD	IRQAHCNISA
98BWM016_d 98BWM036_a	IVCTRPGNN.	.TRKSVRIG.		DIIGD	IRQAHCNISK
98BWM037 d	INCTRPSNN.	.TRKSIRIG.	-	DIIGD	IRQAHCNISE
99BW3932 1	IVCIRPNNN.	.TRKSIRIG.		AIIGN	IREAYCNISG
99BW4642 4	IVCIRPNNN.	.TRKSIRIG.	. PGQTFYATG		IKEAYCNIKE
99BW4745 8	IECIRPNNN.	.TRKSIRIG.	. PGQTFYATG	EIIGD	IRKAHCTINK
99BW4754 7	INCTRPNNN.	.TRKSMRIG.		EIIGD	IRQAHCNISR
99BWMC16 8	ITCTRPNNN.	.TRKSIRIG.	. PGQTFYATG	DIIGD	IRQAHCSINK
A2 CD 97CD	INCTRPNNN.	.TRKSIRFG.	. PGQAFYTNN	NIIGD	IRQAHCNISI
A2_CY_94CY	ITCIRPNNN.	.TRKSIRFG.	.PGQAFYTN.	EIIGD	IRQAHCNINK
A2D97KR	INCTRPDVG.	.QRRSVRIG.	. PGRAFYTRQ	TYTR.QAKGD	IRQAQCNISS
A2G_CD_97C	ITCIRPNNN.	.TRKSIRFG.	. PGQAFYTN .		IRQAYCNISK
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A_KE_Q23_A	IKCIRPNNN.	.TRKSIRIG.	. PGQAFYATG		IRQAHCNVTR
A_SE_SE659	ITCIRPYHN.	.TRTRIHIG.		DIKGS	IRQAHCTVNR
A_SE_SE725	INCTRPSNN.	.TRTSIRIG.	. PGQAFYATG	DITGD	IRQAHCNVSR

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A SE SE853
            INCTRPGNN. .TRKSIRIG. .PGQAFYATG ....EVIGD IRQAHCNVSR
A SE SE889
            IICIRPNNN. .TRKSIRIG. .PGQAFYATG .....DIIGD IRQAYCDVNR
A SE UGSE8
            IICTRPNNN. .TRKSIRIG. .PGQAFYGMG .....DIIGD IRKAHCNVSR
            INCTRPNNN. .TRRSVRIG. .PGQTFYATG .....DIIGD IRQAHCNVSG
A UG 92UG0
            INCSRPYNTR KNIRRYSIG. .SGQAFYVTG .....KIIGD IRQAHCNVSR
A UG U455
            INCTRPNNN. .TRTSIRIG. .PGQTFYTS. ....NIIGD IRQAHCNVSR
AC IN 2130
            INCSRPNNN. .TRKSVHIG. .PGQAFYATG .....DVIGD IRQAYCTVNG
AC RW 92RW
AC SE SE94
            INCTRPGNN. .TRRSVHIG. .PGQAFYATG .....DITGD IRKAHCIVNG
ACD SE SE8
            INCTRPNNN. .TRNSIRIG. .PGQAFYATG ....AITGD IRQAHCNVSR
            INCTRPGNN. .TRKSVRIG. .PGQTFYATG .....DIIGD IRQAHCNISG
ACG BE VI1
            INCTRPNNNT .RK.SVRIG. .PGQALYVTG GII..G...D IRQAFCEVNR
AD SE SE69
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AD SE SE71
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ADHK NO 97
ADK_CD_MAL
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AG_BE_VI11
            INCTRPNNNT RKSIRIGPG. ...QAFYATG EII..G....
AG_NG_92NG
AGHU GA VI
            INCTRPNNNT RKG..IRIG. .PGRVIYATS AIT..G...D IRQAHCNISK
AGU_CD_Z32
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            IKCVRPANNT RKGIHTGPG. ...QVLYATG AVV..GD... IRQAHCNVSR
AJ_BW_BW21
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B AU VH AF
            IKCIRPNNNT .RK.SIHLG. .PGKAWYTTG QII..G...D IRQAHCNLSS
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            INCTRPNNYT .SK.RIRIG. .ARRAFYTKG KII..G...D IRQAHCNISG
B DE D31 U
            INCTRPNNNT .RK.GIHIG. .PGRAVYTTG RIV..G...D IRLAHCNISR
B DE HAN U
B_FR_HXB2_
            INCTRPNNNT .RK.RIRIQR GPGRAFVTIG KIG.....N MRQAHCNISR
B GA OYI__
             INCTRPNNNT .RN.RISIG. .PGRAFHTTK QII..G...D IRQAHCNLSR
B GB CAM1
             INCTRLNNNT .RK.SIAIG. .PGRTVYATD RII..G...D IRQAHCNLSS
            INCTRPNNNT .RK.GIYMG. .PGRRFYTTG RII..G...D IRQAHCNISK
B GB GB8 C
            INCTRPSNNS .RK.SIYIG. .PGRRFHVTR AVT..G...D IRQAHCNISK
B GB MANC
            INCTRLNNNT .RK.SIRIG. .PGSTFYATG AII..G...D IRQAHCNISR
B KR WK AF
            INCTRPNNNT .RK.GIHIG. .PGKAFYATG QII..G...D IRQAHCNLSR
B NL 3202A
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B TW TWCYS
            INCTRPNKKT .RK.RITTG. .PGRVYYTTG EIV..G...D IRQAHCNLSR
B US BC LO
            INCTRPNNNT .RK.GITLG. .PGRVFYTTG EIV..G...D IRKAHCNISK
B US DH123
            INCTRPSNNT .RK.SIHIG. .PGRAFYTTG EII..G...D IRQAHCNISR
B US JRCSF
            INCTRPNYNK .RK.RIHIG. .PGRAFYTTK NII..G...T IRQAHCNISR
B US MNCG
             INCTRPNNNT .RR.RLSIG. .PGRAFYARR NII..G...D IRQAHCNISR
B US P896
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B US RF M1
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            INCTRPNNNT .RK.KITLG. .PGRVLYTTG EII..G...D IRRAHCNLSR
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B_US_WR27_
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INCTRPUNN. TRKSIRIG. PGQAFYATG ...EIIGD IRQAHCNISR
IVCTRPGNN. TRRSMRIG. PGQTFYATG ...EIIGD IR.AHCNISE
B_US_YU2_M
BF1_BR_93B
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C_BW_96BW0
C_BW_96BW1
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CRF01 AE T
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D CD NDK M
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G BE DRCBL
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00BW2127_2 00BW2128 3	EEWNKTLREV		KTIMFA.	.PSSGGDLEI	TAHSFNCRGE
_	NOWNETLORV		KTIMFA.	.OSSGGDLEI	TMHSFNCRGE
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	=		SNIEFK.	.PHSGGDPEI	TTHSFNCRGE
00BW3842_8	GNWTKTLQRV	~	KTIKFO.	.PSSGGDLEI	ATHTFNCRGE
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-	STWNRTLQEV		KTIRFQ.	. PSSGGDLEI	TTHSFNCRGE
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96BW0407	KDWNKTLHRV		KAIKCE.	. PSSGGDLEI	TTHSFNCGGE
96BW0502	TEWNSTLQGV	SKKLEEHFSK	KNITFO.	. PASGGDLEI	TTHTFNCRGE
96BW06_J4	TNWNKTLKGV		KTIGFS.	.OAAGGDLEI	TTHSFNCGGE
96BW11_06	SQWNKTLHRV	IEKLKEHFPN	KTIGFS.	. ESSGGDLEI	TTHSFNCGGE
96BW1210	GAWNETLOWV		KTIEFQ.	. PSSGGDLEI	TTHSFNCGGE
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96BW16_26	SEWKRTLQRV		KTITFA.	.PRSGGDLEI	TTHSFNCGGE
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A2_CY_94CY	THMMDIDÄKA	AEQLREYFSN	KTTTET		TTHSVNCGGE
A2D97KR	YGMMDII OKA	AEQLEKTISN	ΚΝΙΤΤΈ Σ		TTHSTNCGGE
A2G_CD_97C		STQLRKYFNN			TTHSFNCGGE
A_BY_97BL0		AEKLRTYFGN			TTHSFNCGGE
A_KE_Q23_A	SEMNNTI OOV	AKOLRTYFON	KTTTFT	NSSGGDLET	TTHSFNCKGE
A_SE_SE659 A_SE_SE725	SSWNKTLODT	VTQLRVYWN.	RTTIFN	SSSGGDLET	TTHSFNCGGE
A_0B_0B/20	JO.MICI HQD I	Kanter & 1141 +			

```
A_SE_SE753 SKWNATLQKV AIKLREYFDD ...KTIIFT. .KPSGGDLEI TTHSFNCGGE
A_SE_SE853 AKWNKTLHEV AKQLRTYFNN ...KTIIFT. .NSSGGDLEI TTHTVNCGGE
A SE SE889 TEWNEALQKV VNQLKTHFKN ...KTIIFN. .SSSGGDLEI TTHSFNCGGE
A SE UGSE8 SKWNETLKKV AIQLRKYWN. ...TTIIFT. .NSSGGDLEI TTHSFNCGGE
A UG 92UG0 SOWNKTLHOV VEOLRKYWNN ...NTIIFN. .SSSGGDLEI TTHSFNCAGE
            RDWNRTIQQV AEQLKKKFNN ...KTIIFA. .SSSGGDIEI TTHSFNCGGE
A UG U455
            AEWNKALNKI GKQLRKYFVN ...KTIKFA. .NSSGGDLEI TTHSFNCEGE
AC IN 2130
AC_RW_92RW TKWNRTLQKV AEKLSHYFEN ..ITTIIFK. .NSSGGDLEI TTHSFNCGGE
AC SE SE94
            TKWNKTLHKV VTQLRKYFVN ...KPIIFT. .PSSGGDVEV TTHSFNCRGE
            SEWNKTLQQV AKKLGDPLNK ...TEIIFK. .PPSGGDLEI TTHSFNCGGE
ACD SE SE8
ACG_BE_VI1
           KEWNKTLQAV GKKLAEYYPN ...KTINFT. .QASGGDLEI VTHSFNCGGE
            TKWDKTLREV AIQLKHYYG. ..NKTVIFAN .SS.GGDIEI TTHSFNCRGE
AD SE SE69
            SAWNNTLQQV VIQLRRYFNN ...KTIIFT. .NSSGGDLEI TTHSFNCGGE
AD SE SE71
            GSWMKTLHKV ATQLXQHFS. ..NKTIIFNA .SA.GGDIEI TTHSFNCAGE
TEWDKTLQQV AVKLGSLLN. ..KTKIIFNS .SS.GGDPEI TTHSFNCRGE
ADHK_NO_97
ADK CD MAL
            KDWGKMLQEV SRQLKKFFNN ...KTIFFNS .SA.GGDLEI TTHSFNCRGE
AG_BE_VI11
           QEWQEMLQKV QAQLEQVFN. ...KSITFNS .SA.GGDLEI TTHSFNCRGE
EQWNRTLERV KEKLGRHFK. ..NKTITFKP .AS.GGDPEV TMHIFNCRGE
AG NG 92NG
AGHU GA VI
            KEWSETLSKV AAQLRKHFVN T.RTDIIFA. .NSSGGDVEI TTHSFNCGGE
AGU_CD_Z32
           KNWTDTLHKV TAKLKEYFN. ...TTIEFQP .AS.AGDLEI MTHTFNCGGE
AJ BW BW21
           TNWTSVLRQI AVKLRERFK. ..NKTIVFNH .SS.GGDPEI VRHSFNCGGE
B_AU_VH_AF
            TKWNNTLKQI TKKLREQFG. ..NKTIVFNQ .SS.GGDPEI VMHSFNCGGE
B_CN_RL42_
B_DE_D31_U
            AKWDSTLRQI VKKLRERFG. ..NKTIVFNQ .SS.GGDPEI VTHSFNCGGE
B DE HAN U ARWNKTLNQI FRKLREIRQF .ENKTIVFNR .SS.GGDPEI VMHSFNCGGE
B_FR_HXB2_
            AKWNNTLKQI ASKLREQFG. .NNKTIIFKQ .SS.GGDPEI VTHSFNCGGE
B_GA_OYI__
            ATWEKTLEQI ATKLRKQFR. .N.KTIAFDR .SS.GGDPEI VMHSFNCGGE
B_GB_CAM1
            TKWNNTLKQI VTKLKEQFG. ..NKTIIFNQ .SS.GGDPEI VMHSFNCGGE
B_GB GB8 C
           EKWNNTLHQI VIELRKQFR. ..NKTIVFNQ .SS.GGDPEI VMHSFNCGGE
            AKWEKTLKQI VEKLREKFG. ..NKTIIFNQ .SS.GGDPEI VTHSFNCGGE
B GB MANC
B KR WK AF EKWNDTLKQL VIKLGEQFG. .NSNIIVFKQ .SS.GGDPEI VMHSFICGGE
B NL 3202A AKWNNTLKQI VSKLRKQFG. ..NKTIVFSQ .PL.GGDPEI VMHSFNCGGE
B TW TWCYS AEWNNTLPQI VKKFREQFG. ..NKTIVFNQ .SS.GGDLEI VMHSFNCGGE
B US BC LO AKWNDTLRQI VIKLR..EQF .ENKTIVFNQ .SS.GGDPEI VMHSFNCGGE
            VKWHNTLKRV VEKLREKFE. ..NKTIVFNK .SS.GGDPEI VMHSFNCGGE
B US DH123
            AQWNNTLKQI VEKLR..EQF .NNKTIVFTH .SS.GGDPEI VMHSFNCGGE
B US JRCSF
            AKWNDTLRQI VSKLKEQFK. ..NKTIVFNQ .SS.GGDPEI VMHSFNCGGE
B_US_MNCG_
            AKWNNTLQQI VIKLR..EKF .RNKTIAFNQ .SS.GGDPEI VMHSFNCGGE
B US P896
B_US_RF_M1
            AQWNNTLKQV VTKLR..EQF .DNKTIVFTS .SS.GGDPEI VLHSFNCGGE
           AQWNNTLEQI VKKLREQFG. .NNKTIVFNQ .SS.GGDPEI VMHSFNCRGE
B_US_SF2_K
            TSWNNTLKQI VEKLREIKQF .KNKTIVFKQ .SS.GGDPEI VMHSFNCGGE
B US WEAU1
B_US_WR27_
            TKWKNTLEKI VAKIREIKQF .KNKTIVFNH .SS.GGDPEI VMHSFNCGGE
B US YU2 M
            TQWENTLEQI AIKLKEQFG. .NNKTIIFNP .SS.GGDPEI VTHSFNCGGE
            TKWNETLEKV RAKLKPHFPN ...ATIKFNS .SS.GGDLEI TMHSFNCRGE
BF1 BR 93B
            TAWNKTLQEV GKKLAEHFPN ...KAIKFA. .KHSGGDLEI TTHSFNCRGE
C BR 92BR0
            RDWNDTLNRV SKKLAEHFPN ...KTIEFK. .PSSGGDLEI TTHSFNCRGE
 BW 96BW0
            SQWNNTLQRV SEKLKEHFPN ...KTIKFN. .QPAGGDLEI TTHSFNCGGE
C BW 96BW1
            GAWNETLQWV GKKLKEHFPN ...KTIRFK. .ESSGGDLEI TTHSFNCGGE
C BW 96BW1
            GEWNKAVQRV SAKLREHFPN ...KTIEFQ. .PSSGGDLEI TTHSFNCRGE
C BW 96BW1
            EKWNKTLQKV KEKLQKHFPN ...KTIEFK. .PSSGGDLEI TTHSFNCGGE
C ET ETH22
            DKWNETLQRV GKKLAEHFHN ...KTIKFA. .SSSGGDLEI TTHSFNCRGE
C_IN_93IN1
            ENWTDTLQRV SKKLAEHFPN ...KTIKFD. .SPSGGDLEI TTHSFNCRGE
C_IN_93IN9
            DRWNETLQWV GEKLAEHFPN ...KTIKFA. .PSSGGDLEI TTHSFNCRGE
C IN 93IN9
            RDWNETLQRV SEKLAKHFPN ...KTIKFA. .PSSGGDLEI TTHSFNCRGE
DKWNETLQNV SKKLAEHFPN ...KTIIFN. .SSSGGDLEI TTHSFNCRGE
C_IN_94IN1
C_IN_95IN2
            TKWNETLKQV TKKLREHFKN ...KTIIFQ. .PSSGGDPEI TMHHFNCRGE TKWKETLKQV TRKLREHLNG ...TMTISFR .PSSGGDPEI TMHHFNCRGE
CRF01_AE_C
CRF01_AE_C
            TKWNETLQQI IRKLEEHFNN ...KTIQFKP .PYSGGDLEI TMHHFNCRGE
CRF01_AE_C
CRF01_AE_T
            TKWNKVLKQV TEKLKEHFNN ...KTIIFQ. .PPSGGDLEI TMHHFNCRGE
CRF01_AE_T
            TKWNEVLKQV AGKLKEHFNN ...KTIIFK. .PPSGGDLEI TMHHFNCRGE
            TKWNKVLNQV TEKLKEHFNN ...RNISFQ. .PPSGGDLEI TMHHFICRGE
CRF01 AE T
```

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CRF01 AE T
             TKWNETLKQV AGKLREHFNN ...KTIIFQ. .PPSGGDLEI TMHHFNCRGE
             TKWNKVLKQV TEKLKEHFN. ...KTIIFQ. .PPSGGDLEI TMHHFNCRGE
CRF01 AE T
CRF01 AE T
             TKWNKVLKOV TEKLKEHFN. ...KTIIFQ. .PPSGGDLEI TMHHFNCRGG
             SEWNRTLQQV ATQLRKHFN. ...KTIIFA. .NSSGGDIEI TTHSFNCGGE
CRF02 AG F
             SKWNNTLQQV AIQLRKHFN. ...TTIIFA. .NPSGGDIEI TTHSFNCGGE
CRF02_AG_F
             TDWNTTLQQV ATQLGKYFRD T..TRIKFD. .NPSGGDLEI MTHSFNCGGE
CRF02 AG G
CRF02 AG N TEWNKTLHQV VTQLKTYFKN ...TTIIFA. .NPLGGDVEI TTHSFNCGGE
CRF02_AG_S QQWNKTLHDV ATKLREYFNN ...TTIIFD. .EPSGGDLEI TTHSFNCGGE
CRF02 AG S EKWNSTLQKV VTKLGKHFNS ...SKIIFT. .NSSGGDLEI TTHSFNCGGE
CRF03 AB R TKWNNTLKQI VIKLRKQFG. ..NKTIVFNQ .SS.GGDPEI VMHSFNCGGE
CRF03 AB R TKWNNTLEQI VSKLRKQFR. ..NKTIVFNQ .SS.GGDPEI VMHSFNCGGE
CRF04_cpx_ NDWNDTLKVI SEELKRLFP. ..NKTIKFAP .PV.GGDLEI TTHSFNCKGE
CRF04_cpx_ SDWNEALQKV VVKLREHFP. ..NKTIIFNQ .SS.GGDLEI TTHSFNCGGE
CRF04_cpx_ KDWNTTLQKI VDELRKHFP. ..NKNITFAP .SA.GGDVEI TTHSFRLGGE CRF05_DF_B EQWNKTLIQV AKELQSHFP. ..NKTIKFNS .SS.GGDLEI TMHSFNCRGE
CRF05_DF_B AQWNKTLEQV KEELRAHIKD IGNKTIVFNS .SA.GGDLEI TSHIFNCRGE
CRF06_cpx_ ANWTDILGEV KVKLEEVFNN ...THITFKS .SA.GGDLEI TTHSFNCGGE
CRF06_cpx_ KAWNSMLQNV TAKLKELFNN ...KNITFNS .SA.GGDLEV TTHSFNCGGE
CRF06_cpx_
             TAWKETLQNV TEKLKQLLN. ... TNITFNP .SA.GGDLEI TTHSFNCRGE
CRF06_cpx_ TDWNNMLKNV TTKLIEVFK. ...KNITFNS .SA.GGDLEI TTHSFNCGGE
CRF11_cpx_ AEWLNTLQQV ATQLRGKFN. ...KTIIFDN .PSPGGDIEI TSHSFNCRGE
CRF11_cpx_ ADWNNTLQQV AEQLHNNFN. ...KTIVFNE .HS.GGDLEV TTHSFNCGGE
D CD 84ZRO VKWNNTLRQV ARKLGNLLN. ..QTKIIFKP .SS.GGDPEI TTHSFNCGGE
D CD ELI K AQWSKTLQQV ARKLGTLLN. ..KTIIKFKP .SS.GGDPEI TTHSFNCGGE
D CD NDK M AEWNKALQQV ATKLGNLLN. ..KTTITFKP .SS.GGDPEI TSHMLNCGGD
D UG 94UG1 AGWNKTLQQV AEKLGNLLN. ..QTTIIFKP .SS.GGDPEI TTHSFNCGGE
F1 BE V185 TQWNNTLEYV KAELKSHFPN N..TAIKFNQ .SS.GGDLEI TMHSFNCRGE
F1 BR 93BR TQWRNTLAKV KAKLGSYFPN ...ATIKFNS .SS.GGDLEI TRHNFNCMGE
F1 F1 F1 F1 EQWNKTLDRV KAELKLHFNK ....TIQFNS .SS.GGDLEI TMHSFNCRGE
             TOWSKTKTOV QEKLRALFNK ....TIKFNQ .SS.GGDLEI TMHSFNCRGE
F1 FR MP41
F2 CM MP25 KQWYDTLIKI ATEFKDQYN. ...KTVGFQP .SA.GGDLEI TTHSFNCRGE
F2KU BE VI ENWNKTLEGV KAKLHGFFTN ...KTIIFKP .HS.GGDPEV VMHTFNCGGE
             TKWNETLRDV QAKLQEYFIN ...KSIEFNS .SS.GGDLEI TTHSFNCGGE
G BE DRCBL
G NG 92NG0
             IKWREMLKNV TAQLRKIYN. ..NKNITFNS .SA.GGDLEI TTHSFNCRGE
             RKWKEALQNV AAELGKIFNK S.SENITFNS .SA.GGDLEI TTHSFICRGE
G SE SE616
H BE VI991
             KQWNETLHKV ITKLGSYFD. ..NKTIILQP .PA.GGDIEI ITHSFNCGGE
H BE VI997
             EKWNKTLQQI ATQLSKYFV. ..NRTLIFKP .HS.GGDLEV TTHSFNCRGE
H CF 90CF0
             TDWNKTLHQV VTQLGIHLN. ..NRTISFKP .NS.GGDMEV RTHSFNCRGE
J SE SE702 KDWNNTLRRV AKKLREHFN. ...KTIDFTS .PS.GGDIEI TTHSFNCGGE
J_SE_SE788 RDWSNTLRRV ATKLREHFN. ...KTINFTS .PS.GGDIEI VTHSFNCGGE
K_CD_EQTB1 GQWNKTVNQV KKELGKHFN. ...KTIIFQP .SS.GGDPQV TRHIFNCRGE
K_CM_MP535 EKWNMTLSRV KEKLKEHFKN ...GTITFKP .PNPGGDPEI LTHMFNCAGE
N_CM_YBF30 ELWEPMWNRT REEIKKILGK ...NNITFRA RERNEGDLEV THLMFNCRGE
            TDWGKILKQT AERYLELVNN TGSINMTFN. .HSSGGDLEV THLHFNCHGE
TVWENALQQT AIRYLNLVNQ TENVTIIFS. .RTSGGDAEV SHLHFNCHGE
SDWEKALKQT AERYLDLRNN TNTVNITFE. .RSIGGDSEV THLHFNCHGE
SVWEEALKQT AERYLELMNN TNTVNITFN. .HSTGGDPEV THLHFNCHGE
O CM ANT70
O_CM_MVP51
O_SN_99SE_
O_SN_99SE_
U_CD___83C GEWRNTLQQV AIALRRQFNN ... KSIIFN. .SSSGGDIEI TTHTFNCGGE
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	451				500
00BW0762 1		NGTYN	STGD	TNSTN	
00BW0768 2		NKTRR			
00BW0874 2		NSTYN			
00BW1471 2		NSTYN			
00BW1616 2		NGTYN			
00BW1686 8		NETYL			
00BW1759 3		NNTYR			
00BW1733_3 00BW1773 2		NSTYN			
00BW17/3_2 00BW1783 5		NGTYN			
00BW1705_5 00BW1795_6		NGTYN			
00BW1733_0		NGTYM			
00BW1811_5	FEVCNTTHI.F	NGNG		ESD	TNITLPCRIK
00BW1830_3	FEVCOTTRILE	NGTYN	STEO	TN	STITLOCRIK
00BW1880_2 00BW1921 1		NGTYN			
00BW1921_1 00BW2036 1		NSSYN			
00BW2036_1 00BW2063 6		NSSYS			
00BW2083_8 00BW2087 2		N			
00BW2087_2 00BW2127 2	FFICNISGLE	NSTYY	D D	MUK CULL	ETTTI.DCDIK
_		DETQL			
00BW2128_3		NGTYM			
00BW2276_7		NGTYN			
00BW3819_3		NSSYN			
00BW3842_8		NDTYW			
00BW3871_3		NNNLI			
00BW3876_9		NNNLI			
00BW3886_8		NRPNM			
00BW3891_6		NRPNM NNTYR			
00BW3970_2		NNTYR NSTYR			
00BW5031_1					
96BW01B21		NSTYM NESYN			
96BW0407		NSTYS			
96BW0502		DETYL			
96BW06_J4		NSTYI			
96BW11_06					
96BW1210		NSTYN			
96BW15B03		NSSYN			
96BW16_26		NSTYN			
96BW17A09		NSTYN			
96BWM01_5		NGTYN			
96BWMO3_2		NGTYN			
98BWMC12_2		NSTYN			
98BWMC13_4		NGTYS			
98BWMC14_a		NSTYN			
98BWM014_1		NSTYN			
98BWM018_d		NS			
98BWMO36_a		NSTYY			
98BWM037_d		NTSWL			
99BW3932_1		NSTYN			
99BW4642_4		TYQSN			
99BW4745_8	FFYCNTSELF	NSTYN	ANTY	NTATGNNS	TTIILPCRIK
99BW4754_7		NSTFN			
99BWMC16_8		NNTYY			
A2_CD_97CD		NSTWEN			
A2_CY_94CY		NGTWWNN			
A2D97KR		NSTWPAN			
A2G_CD_97C		NSTFNTT			
A_BY_97BL0		NSTX			
A_KE_Q23_A		NSTWY			
A_SE_SE659		NSTWS			
A_SE_SE725	FFYCNTSGLF	NSTWS	у.мрт	GVSNSTES.N	DITITIFCKIK

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FFYCNTSGLF NSTIL..... NSTKM NDNASRESYD DTITLQCRIK
A SE SE753
A SE SE853
          FFYCNTSGLF NSTWS..... SNASE PMSNSTES.N DTITLQCRIR
A SE SE889
         FFYCNTSGLF NSTWN..... GTDSM QKLNST.... GNITLPCRIK
          FFYCNTSGLF NSSWN..... END.T KVNYNTES.N DTITLQCRIK
A SE UGSE8
A UG 92UG0
          FFYCNTSGLF NSTWV..... ....NGTTS STSN..... GTITLPCRIK
A UG U455
          FFYCNTSGLF NSIWN..... GSMSN DMGP....N GTITLQCRIK
AC IN 2130
          FFYCNTSGLF NGTWNASMO. .....ES NSTESN.... ETIILPCRIK
          FFYCNTSGLF NSTWS..... KR NGTWQSNGTE LNITLPCRIK
AC RW 92RW
AC SE SE94
          FFYCDTSGLF NSTWPFNS......T NSTGPN.... GTITLQCRIK
          FFYCNTSGLF NSTWV..... DTITLPCRIK
ACD SE SE8
          FFYCNTSGLF NSTYN..... PSYN STESVN...E TTIILPCKIK
ACG BE VI1
          FFYCNTTGLF NSTWNDTAT. .....EQKP ......N.. DTIRLQCRIK
AD SE SE69
          FFYCNTSGLF NSTWN..... NTDSM QESHSTET.N DTITLPCRIK
AD SE SE71
          FFYCNTSQLF NSTWNHTST. .....YNST EN..... GTITLPCKIK
ADHK NO 97
          FFYCNTSKLF NSTWQNNGA. .....RLSN S..TE.ST.. GSITLPCRIK
ADK CD MAL
          FFYCNTSALF NFSSETNST. ..... FP.N.... TTLTLPCRIK
AG BE VI11
AG NG 92NG
          AGHU GA VI
AGU_CD_Z32
          FFYCNTSGLF NSTWK..... NSTSI NDTVSN.... GTITLPCRIK
          FFYCNTSGLF NKSLLNETS. .....NETT DGAN..... NTITLTCRIK
AJ BW BW21
B_AU_VH_AF
          FFYCNSTQLF NSTWFNSTG. .....NDTE RATNN..T.. ENITLPCRIK
          FFYCNTSQLF NSTWNDTG.. ..........T WNDTTGNS.. .TITLPCRIK
B_CN_RL42
          FFYCNSAQLF NSTWNDTK......ES NNTNG......TITLPCRIK
B DE D31 U
          FFYCNSTKLF NSTWNNTST. ..... DNGND..... TIILPCRIK
B DE HAN U
B FR HXB2_
          FFYCNSTQLF NSTWFNSTW. .....STEG SNNTEGSD.. .TITLPCRIK
          FFYCNTSQLF NSTWNDTTR. .....AN.. .STEV..... .TITLPCRIK
B GA OYI__
          FFYCNTTQLF NTTWLFNGT. .....WNDT EGLNNTER.. .NITLPCRIK
B GB CAM1
          FFYCKTAQLF NSTWNSTGN. .....GTIK SNTTE..... .IITLPCRIK
B GB GB8 C
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B GB MANC
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B KR WK AF
          FFYCNSTQLF NSTWNDTGN. .....VTER SNNNE..... .NITLPCRIK
B NL 3202A
          FFYCNATPLF NSTWNATST. .....LNAT NEENE..... .NITLLCRIK
B TW TWCYS
          FFYCKSTQLF NSTWAGNNT. .....WNSS AERSDDTG.. GNITLPCRIK
B US BC LO
          FFYCNTKKLF NSTWNGTEG. .....SYNI EGND..... .TITLPCRIK
B US DH123
          FFYCNSTQLF NSTWNDTEK. .....SSG. TEGND..... .TIILPCRIK
B US JRCSF
          FFYCNTSPLF NSTWNGNNT. .....WNNT TGSNN..... .NITLQCKIK
B US MNCG
          FFYCNTAQLF NSTWNVTGG. .....TNG. TEGND..... .IITLQCRIK
B US P896
          FFYCNTTQLF NSTWNSTEG. .....SNNT GGND..... .TITLPCRIK
B US RF M1
B US SF2 K
          FFYCNTTQLF NNTWRLNHT. .....EG.. TKGND..... .TIILPCRIK
          FFYCNSTQLF NSTWHANGT. .....WKNT EGADN..... .NITLPCRIK
B US WEAU1
          FFYCNSTQLF NSTWNSTEG. .....NS.. TWSDK..... . IIRLPCRIK
B US WR27
B US YU2 M
          FFYCNSTQLF ...TWNDTRK. .....LN.. .NTGR..... .NITLPCRIK
          FFYCNTSGLF NDTVDN.... GTITLPCRIK
BF1 BR 93B
          FFYCNTSSLF NSTYT..... PNST ENITGT..EN SIITIPCRIK
C BR 92BR0
          FFYCNTSRLF NESYS..... FNES HWSND...TN ATITLPCRIK
C_BW_96BW0
          FFYCNTSKLF NGTYI..... QPNS .TEDTP...N STITLPCRIK
C_BW_96BW1
          FFYCNTSQLF NSTYN..... S.TY MPS...NNTG TNITLQCRIK
C_BW_96BW1
          FFYCNSSKLL NSSYN..... GTSY RGTESN...S SIITLPCRIK
C_BW_96BW1
          FFYCNTSNLF NSTKL..... LFNSS...TN LNITLQCRIK
C_ET_ETH22
          FFYCNTSGLF NGTYM..... PTYM PNGTESN.SN STITIPCRIK
C IN 93IN1
          FFYCNTSGLF NGTYN..... TSSD GNS.....S STITIPCRIK
C IN 93IN9
          FFYCNTSSLF DSLFN..... PNGT RNDT....N LTITIPCRIK
C IN 93IN9
          FFYCNTSGLF NSTYM..... SGTY MNSSADM.NS SYITIPCRIK
C_IN_94IN1
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C IN 95IN2
          FFYCNTTKLF NSTWT..... TNE IMEEFKGTNS STITLPCRIK
CRF01 AE C
          FFYCNTTALF NSTWI..... N.G TMQEVNGTNS GNITLPCRIK
CRF01 AE C
          CRF01_AE_C
          FFYCNTTQLF NNTCI......GNE TMK...GCNG .TITLPCKIK
CRF01 AE T
          FFYCNTTQLF NSTWT......GNE TME...GSNG .TITLPCKIK
CRF01 AE T
          FFYCNTTRLF NNTCI......GNK TMK...ECND .TIILPCKIK
CRF01 AE T
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FFYCNTTKLF NSTWI..... GNE TIG....SSG .NIILPCRIK
CRF01 AE T
          FFYCNTTKLF NNTCL......GNE TMA...GCND .TITLPCKIK
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          FFYCNTTKLF NSTWR..... GNE TIESREGYNK .TIILPCKIK
CRF01 AE T
          FFYCNTSELF NSTW..... ..NSTWDNSS NHIESNHT.E GNITLQCRIK
CRF02 AG F
          FFYCNTSELF N...... STWDNSL NHTESNHT.E DNITLQCRIK
CRF02 AG F
         FFYCNTSGLF NSTWYKN... ..STWYSNST ASSNHTEL.N STITLQCKIK
CRF02 AG G
         FFYCNTSKLF N...... STWDNSN STANHTGS.N DTITLQCRIK
CRF02 AG N
         FFYCNTSNLF NRTWNHNGTW NAPGPFNDTE DKTINGTE.D KTITLQCRIK
CRF02 AG S
CRF02 AG S
         FFYCNTAELF NSTWASN... .TNGIWASNI NASNNKDA.N DTITLKCKIK
CRF03 AB R FFYCNTTKLF NSTWNGTEE. .....LN.. .NTEG..... DIVTLPCRIK
CRF03_AB_R FFYCNTTKLF NSTWNNTEE. .....SN.. .NTKG..... DIVTLPCRIK
          FFYCNTTPLF NSTHMQNGT. .....NIT. S.TDSTN... STITLQCRLK
CRF04 cpx
          FFYCNTSGLF NSTYMFNST. .....NRTN T.TNGTN... STITLPCRIK
CRF04 cpx
          FFYCNTSDLF NRTYMVNKN. .....ETNS T.NTTDE... KIIRLPCRIK
CRF04_cpx_
CRF05 DF B FFYCDTSKLF NATVFNDTV. .....FNAT MFNND...SD KNIILPCKIK
FFYCNTSNLF NTSDLFNTS. .....R..G NDTN..... TTITLPCKIK
CRF06_cpx_
CRF06_cpx_ FFYCNTSQLF NNNITDSNE. . . . . . . . . . . . . TNFTLPCKIK
FFYCNTSGLF NSTWYANDN. .....TSTQ NDMQSN...D .TITLPCRIK
CRF11_cpx_
D CD 84ZRO FFYCNTSGLF NSAWNISGH. .....STGL N.....D.. TIITIPCRIK
D_CD_ELI_K FFYCNTSGLF NSTWNISAW. .....NNIT ESNNS.TN.. TNITLQCRIK
D_CD_NDK_M FFYCNTSRLF NSTWNQTNS. . . . . . TGFN . . . . . . . . . GTVTLPCRIK
         FFYCNTTRLF NSTWKRNNS. .....EWRS D..NT.PD.. ETITLQCRIK
D UG 94UG1
         F1 BE VI85
         FFYCNTDELF NDTKFND... .....TG...FN GTITLPCRIK
F1 BR 93BR
         FFYCNTSLLF NNTVPN.... GTITLPCRIK
F1 FI FIN9
          FFYCDTSGLF NESEKY.... ......N GTIILPCKIK
F1 FR MP41
          FFYCNTTILF NHTRVNDIL. .....SNNH TR.....EN DTITLPCRIK
F2 CM MP25
F2KU BE VI
          FFYCNTTRLF NDTLNHT......ID QNITLPCKIK
         FFYCNTSGLF NNSILKSNI. ..... SENN..... DTITLNCKIK
G BE DRCBL
G NG 92NG0
         FFYCNTSGLF NNNISNIN............................ ETITLPCKIK
          FFYCNTSGLF NSSLLRSNS. ..... SE.N.... GTITLPCKIK
G SE SE616
          FFYCNTTKLF NSTWTNSSY. .....TNDT YNSNSTEDIT GNITLQCKIK
H BE VI991
          FFYCNTSGLF NSSWTGDNI. .....NMPN DTG..... KNITLPCRIK
H BE VI997
          FFYCNTSGLF NSSWEMHTN. .....YTSN DTKG...N.. ENITLPCRIK
H CF 90CF0
          FFYCNTSTLF NSSWDENNI. .....KDTN STNDN..... TTITIPCKIK
J SE SE702
          FLYCNTSKLF NSSWDKNSI. .....EATN DTSX..... ATITIPCKIK
J SE SE788
K CD EQTB1
          FSYCDTTDTV DDTEEE.... ....... ED TTITIPCRIK
K CM MP535
          FFYCNTTKLF NETGE..... GTITLPCRIK
          FFYCNTSKLF NEELLN.... ETG. .... EPITLPCRIR
N CM YBF30
          FFYCNTAKMF NYTFS..... CNGTTC SVSNVSQ.G. NNGTLPCKLR
O CM ANT70
          FFYCNTSGMF NYTFIN.... CTKSGC QEIKGSNETN KNGTIPCKLR
O CM MVP51
          FFYCNTSKMF NYTFS..... CIGTNC TSNQNSSNS. NDTRIYCRIK
O SN 99SE_
          FFYCNTSQMF NYTFS..... CTRTNC IRQSNSS... INGTISCRIK
O SN 99SE
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U CD 83C
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00BW1921 1				LLLTRDGGKG	
00BW2036 1		RGIYAPPIEG			INTSTVE
00BW2063 6	~ ~	RAMYAPPIAG			NETNETE
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96BW0502				LLLTRDGGKT	
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96BW11_06				LLLTRDG	
96BW1210				ILLVRDGGNT	
96BW15B03				LLLARDGG	
96BW16_26				LLLVRDGGTE	
96BW17A09				LLLTRDGGK.	
96BWM01_5				LLLTRDGG LLLTRDGGKT	
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98BWMC13_4	QIINMWQGVG	DATVADDIKC	NITCISNITG	LILTRDGG LLLTRDGGSN	סייי די
98BWMC14_a				ILLTRDGGIN	
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98BWMO36_a 98BWMO37 d				LLLENDG	
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A BY 97BL0	QIINMWQRVG	QAMYAXPIKX	SIRCESNITG	LLLTRDGXGX	TNXSNE
A KE Q23 A	QIINMWQRAG	QAMYAPPIPG	VIKCESNITG	LLLTRDGGKD	NN VNE
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A SE UGSE8
A UG 92UG0
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A UG U455
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AC IN 2130
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AC RW 92RW
AC SE SE94
           QIIRMWQRTG QAIYAPPIPG EINCVSNITG LLLTRDG..G NNI....TNE
ACD_SE SE8
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B_FR_HXB2_
B GA_OYI__
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B KR WK AF
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C_BW_96BW1
C_ET_ETH22
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C IN 93IN9 QIINMWQEVG RAMYAPPIEG NITCKSNITG LLLVRDGGAE AK...TNNTE
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           QIVNMWQEVG RAMYAPPISE VINCVSNITG ILLTRDGGIN QNQTNK..NE
CRF01 AE C
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CRF01 AE T QIINMWQGAG QAMYAPPING TINCISNITG ILLTRDGGD. NNNTI...NE
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CRF02 AG S QIVRMWQKVG QAMYAPPIPG EIRCESNITG LLLTRDG.GN DNN....NTE
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O CM ANT70
O CM MVP51 QLVRSWMKGE SRIYAPPIPG NLTCHSNITG MILQLDQPWN STGE....N
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96BW11 06		DNWRSELYKY			
96BW1210		DNWRSELYKY			
96BW15B03	IFRPOGGDMK	DNWRNELYKY	KVVEIKPLGV	APTEAKRRVV	EREK.R
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A BY 97BL0		NNWRSELYKX			
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A SE UGSE8
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A UG 92UG0
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A SE UGSE8 IKRVRQGYSP LSFQIHTP.. SPR.DPDRPG RIEEEGGEQG RDRSIRLVSG
A UG 92UG0 INRVRQGYSP LSFQTHTP.. NPR.GLDRPG RIEEEGGEQD RGRSIRLVSG
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A UG U455
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C BW 96BW1
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D CD NDK M
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CRF02 AG S FLALAWDDLR SLCLFSYHRL RDFVSIVART VELLGHR.....GWEALK
CRF02 AG S FLALAWDDLR SLCLFLYHRL RDFVLIAART VELLGHSSLK GLRLGWEALK
CRF03_AB_R FLALIWDDLR SLCFFIYHHL RDLLLIAARI VELLGRR.......GWEALK
CRF03 AB R FLALIWDDLR SLCLFIYHHL RDLLLIAART VELLGRR........GWEALK
           FLPLIWDDLR NLCLFSYRHL RNLLLIVART VELLGIR.....GWEALK
CRF04 cpx
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           FLPLVWDDLR NLCLFSYRQL RNLLLIVAKT VELLGIR.....GWGTLK
CRF04_cpx_
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           LSTLIWDDLR NLCLFSYHRL RDLILIAARI VELLGRR........GWEALK
CRF05_DF_B
           FLALAWDDLR SLCLFSYHRL RDFGLIAART VEILGRR.......GWEILK
CRF06_cpx_
CRF06_cpx_ FLALAWDDLR SLCLFSYHRL RDFVLIAART VGTLGHR.......GWEILK
           FLALAWDDLR SLCLFSYHRL RDFVLIAART VETLGRR......GWEILK
CRF06_cpx_
CRF06_cpx_ FLALAWEDLR SLCRFSYHLL RDFVLIVLRT VETLGHR......GWEILK
           FLAIAWDDLR NLCLFSYHRL RDFILIVARI VETLGHR... ....GWEILK
CRF11_cpx_
           FLALAWDDLR NLCLFLYHQL RDFILIVARI VETLGRR......GWESLK
CRF11_cpx_
D CD 84ZR0 FSALIWDDLR NLCLFSYHRL RELILIAARI VELLGRR.......GWEALK
D CD ELI K FSALIWDDLR SLCLFSYHRL RDLILIAVRI VELLGRR... .... GWDILK
D CD NDK M LFALFWDDLR NLCLFSYHRL RDSILIAARI VELLGRR......GWEALK
D UG 94UG1 LSALIWDDLR NLCLFSYHRL RDLILIAARI VELLGRR......GWEAIK
F1 BE VI85 FLALAWDDLR NLCLFSYRHL RDFILIAARI VDRGLRR........GWEALK
F1 BR 93BR FLALAWDDLR NLCLFSYRHL RDFILIAARI VDRGLKR......GWEALK
           FLALVWDDLR NLCLFSYRHL RDFILIAARI VDRGLRR.......GWEALK
F1 FI FIN9
           FLSLVWDDLR NLCLFSYRHL RDFILIAART VDRGLTR.....GWETLK
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           FLALAWDDFR SLCVFSYHCL RNFILIAART VDKGLKR....GWEVLK
F2 CM MP25
           FLALAWDDLR NLCLFSYRHL RDLILIVARI LERGLRG.....SWEILK
F2KU BE VI
G BE DRCBL
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           FLALAWDDLR SLCLFSYHRL RDLVLIAART VELLGRSSLK GLRLGWEGLK
G NG 92NG0
           FLPLIWDDLR SLCLFSYHRL RDSILIVART VELLGRSSLK GLRLGWEGLK
G SE SE616
           FLPLVWEDLR NLCLFSYRRL RDLLSIVART VELLGRR.....GWEALK
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           FLPIVWDDLR SLCLFSYRLL RDSLLIVIRT VELLGRR.......GREALK
H BE VI997
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J SE SE788
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K CD EQTB1
           FLALAWDDLR NLCLFSYRQL RNLILIVTRI LERGLRG......GWEALK
K CM MP535
N CM YBF30 FSALVWEDLR NLLIFLYHRL TDSLLILRRT LELLGQSLSR GLQLLNELRT
O CM ANT70 FLPLLYTDLR TIILWTYHLL SNLASGIQKV ISYLRLGLWI LGQKIINVCR
           FLQQLYTDLR TIILWTYHLL SNLISGIRRL IDYLGLGLWI LGQKTIEACR
O CM MVP51
           FLPLLYTDLR TIILWSYHLL SNLASGIQTV ISHLGLGLWT LGQKIISACR
O_SN_99SE_
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U_CD___83C FLALAWEDLR SLCIFSYHRL RDLILIVVKG ...LRR.... ....GWEALK
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901 00BW0762 1 YLGILVOYWG LELKKSAISL FDTIAIAVAE GTDRIIEAIQ RICRAICNIP YLGNLVLYWG LELKKSAISL LDSIAIAVAE GTDRILEAVQ RIWGAIRNIP 00BW0768 2 YLGSLVQYWG LELKKSAISL LDTIAIAVAE GTDRIIELIQ RICRAIYNIP 00BW0874 2 00BW1471 2 YLGSLGQYWG QELKKSAINL FDTIAIAVAE GTDRIIEAVQ RAVRAILHIP 00BW1616 2 YLGSLVQYWG LELKKSAVSL LDTIAIAVAE GTDRILEVTQ RICRVIRNIP 00BW1686 8 YLGSLIQYWG LELKKSAISL LDTIAIAVAG GTDRFIELIQ RIYRAIRNVP 00BW1759 3 YLGSLGQYWG LELKKSAISL LDTIAIAVAE GTDRIIELIQ TICRAIRNIP 00BW1773 2 YLGNLVQDWG LELKKSAISL FDAIAIAVAE GTDRIIELIQ RTGRAICNIP 00BW1783 5 YLGTLVQYWV LELKKSAISL LDATAITVAG GTDRIIELIQ RIGRAILSIP 00BW1795 6 YLGSLVQYWG LELKKSAISL LDTVAIAVAE GTDRIIELIQ RGYRAICNIP 00BW1811 3 YLGSLVQYWG LELKKSAISL LDTIAIAVGE GTDRIIEIIQ RICRAIRNTP 00BW1859_5 YLGSLVQYWG LELKKSAISL LDTIAIAVAE GTDRIIDLIQ RICRAILRIP 00BW1880_2 YLGSLIQYWG LELKKSAISL LDTIAIAVAE GTDRIIEGIQ RICRIIRNIP 00BW1921_1 YLGSLIQYWG LELKKSAISL LDTIAIATAE GTDRIIEVIQ RICRVIRNIP 00BW2036_1 YLGSLVQYWG LELKKSAISL LDTIAIAVAE GTDRIIELVQ RIGRGIYNIP 00BW2063_6 YLGSLVQYWG LELKKSAISL LNTTAIAVAE GTDRVIELLQ RIGRAICNIP 00BW2087_2 YLGSLVQYWG LELRKSASSL LDTIAIAVAE GTDRIIEVIQ IICRAILHIP 00BW2127_2 YLGNLVLYWG LELKKSAISL FDTIAVAVAE GTDRILEVIQ RICRAIRNIP 00BW2128_3 YLGSLVQYWG LELKKSAVSL LNTIAIVVAE GTDRILELIQ RLRRAFLNIP 00BW2276_7 YLGNLAQYWG LELKKSAISL INTIAIAVGE RTDRIIELIQ TLCRAIHNIP 00BW3819_3 YLGNLVQYWG LELKRSAISL LDTIAIAVAE GTDRIIEFLQ RIFRAIRNIP 00BW3842_8 YLGNLVQYWG LELKKSAISL LDAIAIAVGE GTDRILELLQ RIGRGICNIP 00BW3871_3 YLGSLIQYWG LELKKSAINL LDTTAIAVAE GTDRFIELIQ RICRAVRNIP 00BW3876_9 YLKNLGLYWG LELKKSAISL LNTIAIAVAE GTDRVIEFVL RICRAIRHIP 00BW3886 8 YLGSLVQYWG LELKKSATSL LDTIAIAVAE GTDRIIETVL RICRAILHIP 00BW3891 6 YLGSLVQYWG LELKKSAISL LDTIAIVVAE GTDRIIELVL GICRAIRNVP 00BW3970 2 YLASLVQYWG LELKKGAISL LDSIAIAVAE GTDRIIAFIQ RLFRAICNLP 00BW5031 1 YLGSLVQYWG LELKKSAISL LDTIAIAVAE GTDRIIEVVQ RLYRAILNIP 96BW01B21 YLGNLLLYWG LEPKKSAINL LDTTAIAVAE GTDRILELVQ GICRAIRNIP 96BW0407 FLGSLVOYWG LELKKSAISL LDTTAIAVAE GTDRIIEIAQ RICRAICNVP 96BW0502 YLGSLVOYWG LELKKSAISL LDTIAIAVAE GTDRIIEFIQ RICRAIRNIP 96BW06_J4 YLGSLIQYWG LELKRSTISL LDTVPIAVPE GTDRIIELIQ RIWRAICNIP 96BW11_06 YLGSLVQYWG LELKKSAISL LDTTAIAVAE GTDRIIEVLQ RIGRAIRNTP 96BW1210 YLGSLVQYWG LELKKSAISL LDTIAIAVAE GTDRIIELTQ RVFRAIRNIP 96BW15B03 YLGSLVQYWG LELKKSATSL LDSIAIAVAE GTDRIIEVIQ RIYRAFCNIP 96BW16_26 YLGSLVQYWG LELKKSAINL LDTIAIAVAE GTDRIIDFIL RICRAIRNIP 96BW17A09 YLGSLGQYWG QELKKSAINL LDTIAIAVAE GTDRIIEVLQ GAIRAILNIP 96BWMO1 5 YLGSLVQYWG LELKKSAISL LDTTAIAVAE GTDRIIEVLQ RVGRAIRNTP 96BWMO3_2 YLGSLVRYWG LELKKSAISL LDTIAVAVAE GTDRIIEVIQ GICRGIRNIP 98BWMC12 2 YLGSLVQYWG LELKKRAISL LDTTAIAVAE GTDRIIEIVL RICRAICNVR 98BWMC13 4 YLGSLVQYWG LELKKSAISL LDTTAIAVAE GTDRIIELLQ RIGRAIRNTP YLGNLIQYWG LELKKSAINL LDTLAIAVAE GTDRIIELIQ RVCRAILNIP 98BWMC14_a YLGNLVQYWG LKLKKSAISL FDTIAIAVAE GTDRIIELIQ IICRAIRNIP 98BWMO14_1 98BWMO18_d YLGSLVQYWG LELKKSAISL LDTIAIAVAE GTDRIIELVQ RICRGVLNIP 98BWMO36_a YLGSLVQYWG LELKKSAISL LDTIAIATAE GTDRIIELIQ RICRAIYNIP 98BWMO37_d YLGNLVQYWG LELKKSAISL LDTIAIAVAE GTDRIIEFIQ RICRAIRNLP 99BW3932_1 YLGSLVOYWG LELKKSAISL LDATAVAVAE GTDRILEIIQ RIFRAICNIP 99BW4642_4 YLGSLVQYWC LELKKSATSL IDAIAIAVAE GTDRIIDLIQ RICRAIRNIP 99BW4745_8 YLGSLVQYWG LELKKSAISL FDTIAIAVAE GTDRIIELVL RICGAIRNIP 99BW4754_7 YLGSIVQYWG LKLKKSAISL LDTTAIAVAE GTDRIIELLR RFCRAIYSIP 99BWMC16_8 YLGSLGQYWG LELKKSAIGL LDTIAIAVAE GTDRIIELIQ RTFRAICNIP A2_CD_97CD HLWNLLVYWG QELKTSAIRL LDTIAVAVAE WTDRVIEIGQ RACRAIRNIP A2 CY 94CY NLWNLLLYWG RELKNSAISL FDTIAVAVAE WTDRVIEIGQ RAFRAILNIP A2D___97KR YLWNLLLYWG RELKNSAISL FNATAIAVAE WTDRVIEIVQ RACRAIINIP A2G_CD_97C YLWNLLLYWG QELKNSASNL LDTVAIAVAN WTDRVIEAAQ GACRAIRNVP A_BY_97BL0 YXXNLXGYXG QELKSSAINL IDTIAIAVAX XTDXVIEIGQ RFCRAIRNIP A_KE_Q23_A YLWNLLSYWG RELKISAINL VDTIAIAVAG WTDRVIEIAQ RIGRAILHIP A_SE_SE659 YLGNLLLYWG RELKISAINL LDTTAIAVAG WTDRVIEIVQ GIGRAFLHIP A_SE_SE725 YLGNLLLYWG QELKLSAISL FDTPAIAVAG WTDRGIELIQ RIGRAILNIP

YLWNLLLYWG RELKSSAINL VDTIAIAVAG WTDRIIEIGL RIGRAFLHIP A SE SE753 A SE SE853 YLWNLLVYWI RELKISAISL LDTIAIAVAG WTDRVIELGQ RLCRAILHIP A SE SE889 YLKNLLSYWG RELKLSAINL LDTIAIVIAG WTDRVIEIGQ GFCRAIFHP. YLGNLLLYWI RELKISAISL FDTIAIAVAG WTDRVIEIGQ RIGRAILHIP A SE UGSE8 A UG 92UG0 YLGNLLLYWG RELKISAINL LDTIAIAVAG WTDRVIETVQ RLGRAILNIP YLWNLLLYWG RELKISAITL LDAVAVAVAG WIDRVIEIGQ TIGRAILNIP A UG U455 AC IN 2130 YLWNLLVYWG RELKISAIKL VDTIAIVVAG WTDRIIEIGO GIGRAILHIP AC RW 92RW YLGNLVQYWG LELKRSAINL LDTTAIVVAE GTDRIIELIQ RISRAIYNIP AC SE SE94 YLWNLLLYWG RELRISAINL LDTIAIATAS WTDRVIELGQ RICRAILNIP YLWNLLQYWI QELKNSAINL FNTIAIAVAE GTDRVIEIGQ RIGRAILNTP ACD SE SE8 LLGNILLYWS QELKNSAINL LDTIAIAVAN WTDRVIEIGQ RAGRAFLNIP ACG_BE_VI1 YLWNLLQYWI QELKNSAISL VDTTAIAVAE GTDRVIETVQ RAFRAVLRIP AD SE SE69 YLWNLLQYWI QELKISAISL VDSIAIVVAG WTDRVIEIGQ GIGRAILHIP AD SE SE71 YLGNLLLYWG QELKNSAINL LNTTAIAVAE GTDRIIEIVQ RTGRAVLHIP ADHK NO 97 YLWNLLQYWG QELKNSAISL LNTTAIAVAE CTDRVIEIGQ RFGRAILHIP ADK CD MAL YLWNLLVYWG QELKNSAINL LDTVAIAVAN WTDRVIEIGQ RAGRAILNIP AG BE VI11 YLWNLLLYWG RELKNSAINL IDTIAIAVAN WTDRVIEVAQ GACRAILNIP AG_NG_92NG AGHU GA VI YLWNLLLYWG QELKSSAISL LDAVAIAVAN WTDRVIEVVQ RVGRAILNIP AGU_CD_Z32 YLGNLVIYWG QELKNSAINL LDTVAIAVAD WTDRVIEVVQ RAGRAFLNIP AJ_BW_BW21 YLGNLALYWG RELKNSAISL LDTIAITVAE ATDRIIEIAQ RAFRAILHIP B_AU_VH_AF YWWNLLQYWS QELQNSAISL LNATAIAVAE GTDRVIEVVQ RACRAILHIP YWWNLLQYWI QELKNSAIGL LNATAIAVAE GTDRVIEVVQ RAYRAILHIP B_CN_RL42_ B_DE_D31_U YWWNLLQYWS QELKNSAVSL LNATAIAVAE GTDRVIEVVQ RAWRAILHIP YWWNLLQYWS QELKNSAVSL FNTIAIAVAE GTDRVIEVVQ RACRAILHIP B_DE_HAN_U YWWNLLQYWS QELKNSAVSL LNATAIAVAE GTDRVIEVVQ GACRAIRHIP B_FR_HXB2_ B_GA_OYI__ YWWNLLQYWS QELKNSVISL LNATAIAVAE GTDRVIEIVQ RAYRAFLNIP YWWNLLQYWS QELRNSAVSL FDTIAIAVAE GTDRVIEVVQ RACRAILHIP B GB CAM1 YWWNLLQYWI QELKNSAISL LNTTAIAVAE GTDRVIEVVQ RAYRAILHIP B GB GB8 C YWWNLLQYWS QVLKNSAVSL LNVTAIAVAE GTDRIIEVVQ RVGRAILHIP B GB MANC YLWNLLQYWS QELKNSAVSL LNATAVAVAE GTDRIIEILQ RAYRAILNIP B KR WK AF YWWNLLOYWS QELKNSAVSL LNATAIAVAE GTDRVIEVVQ RACRAVLHIP B NL 3202A YLWNLLOYWI QELKNSAVSL FNAIAIAVAE GTDRVIEVVQ RVFRAILHIP B TW TWCYS B US BC LO YWWSLLQYWS QELKNSAVNL LNVTAIAVAE GTDRVIEVVQ RTYRAILHIP YLWNLLQYWS QELKNSAVSL LNATAIAVGE GTDRIIEILQ RAGRAILNIP B US DH123 B US JRCSF YWWNLLQYWS QELKNSAVSL LNATAIAVAE GTDRIIEVVQ RVYRAILHIP B US MNCG YWWNLLQYWS QELKSSAVSL LNATAIAVAE GTDRVIEVLQ RAGRAILHIP B US P896 YWWNLLQYWS QELKNSAVSL LNATAIAVAE GTDRVIKIVQ RACRAIRNIP YWWNLLQYWS QELKNSAVSL LNTTAIAVAE GTDRIIEVAQ RILRAFLHIP B US RF M1 B US SF2 K YWWSLLQYWI QELKNSAVSW LNATAIAVTE GTDRVIEVAQ RAYRAILHIH B_US_WEAU1 B_US_WR27_ YWGNLLQYWG QELRNSAISL LNATAIAVAE GTDRVIEVGQ RIFRAILHIP B US YU2 M YWWNLLQYWI QELKNSAVSL LNATAIAVAE GTDRVIEILQ RAFRAVLHIP BF1 BR 93B LLGNLALYWS QELKNSAISL LNTTAIVVAE GTDRVIEALQ RAGRAVLNVP YLGGLVQYWS LELKKSAISL FDTIAIAVAE GTDRIIEVIQ GIWRAICNIP C BR 92BR0 FLGSLVQYWG LELKKSAISL LDTTAIAVAE GTDRIIEIAQ RICRAICNIP BW_96BW0 C BW 96BW1 YLGSLVQYWG LELKMSTISL LDTTAIAIAE GTDRIIELIQ RIGRAIRNTP YLGSLVQYWG LELKKSAISL LDTIAIAVAE GTDRIIELTQ RVFRAIRNIP C_BW_96BW1 _BW_96BW1 YLGSLVOYWG LELKKSATSL LDSIAIAVAE GTDRIIEVIQ RIYRAFCNIP YLGSLVQYWG LELKKSAINL LNTTAIVVGE GTDRFIELIQ RIWRAFCNIP C_ET ETH22 YLGSLVQYWG LELKKSAISL FDSIAIVVAE GTDRIIELVQ GFCRAIRNIP C_IN_93IN1 YLGSLVQYWG LELKKSAISL LDIIAIAVAE GTDRIIELIQ RTCRAIRNIP C_IN_93IN9 C_IN_93IN9 YLGSLVQYWG IELKRSAISL LDFTAIAVAE GTDRIIELVL RICRAIRNIP YLGSLVQYWG LELKKSAIRL LDIIAIAVAE GTDRIIEIIQ GTCRAIRNIP C IN 94IN1 YLGSLVQYWG LELKKSAINL LDRIAIAVAE GTDRILELVQ RICRAIRNIP C IN 95IN2 YLGNLLSYWG QELKTSAITL FDAIAVAVAG WTDRVIEVVQ RAWRALIHIP CRF01_AE_C YLGNLLSYWV QELRISAITL LDATAITVAG WTDRVIEIVQ RAWRAILHIP CRF01_AE_C CRF01_AE_C YLGSLLSYWG QELKTSAITL LDATAITVAG WTDRAIEIAQ RACRAILHIP YLGNLLLYWG QELKISAISL LNTTAIAVAG WTDRVIEVAQ GAWRAILHIP CRF01_AE_T YLGNLLLYWG QELKISAISL LDATAIAVAG WTDRVIEVAQ GAWRAILHIP CRF01_AE_T YLGNLLLYWG QELKISAISL FDALAVVVAG WTDRVIEVAQ GAWRAILHIP CRF01 AE T

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00BW1795 6	TRIRQGFEAA	LQ
00BW1811 3	RRIRQGFEAS	LL
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_		ΓΓ
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96BW17A09	TRIRQGLEAA	LQ
96BWMO1_5	RRIRQGFEAA	LL
96BWMO3_2	RRIRQGFEAA	LL
98BWMC12_2	GFEAA	LQ
98BWMC13_4	RRIRQGFETA	LL
98BWMC14_a	RRVRQGFEAA	_
98BWMO14_1	TRIRQGLEAA	
98BWM018_d	RRIRQGFEAA	
98BWMO36_a	TRIRQGFEAA	
98BWM037_d	RRIRQGFEAA	$_{ m LL}$
99BW3932_1	RRIRQGFETA	LL
99BW4642_4	RRIRQGFEAA	LQ
99BW4745_8	TRIRQGFEAA	LQ
99BW4754_7	RRIRQGFEAA	LQ
99BWMC16_8	RRIRQGFETA	LL
A2_CD_97CD	RRIRQGLERA	
A2_CY_94CY	RRIRQGLERA	LL
A2D97KR	RRIRQGLERA	
A2G_CD_97C	RRIRQGLERA	LL
A_BY_97BL0	RRIRXGAEKA	
A_KE_Q23_A	VRIRQGLERA	LL
A_SE_SE659	RRIRQGFERA	LL
A_SE_SE725	RRIRQGFEEA	LL

A SE SE753	RRIRQGFERA	LL
A SE SE853	VRIRQGFERA	LL
A_SE_SE889	RRSKQGLKRA	LQ
A_SE_UGSE8	RRIRQGFER.	
A_UG_92UG0	RRIRQGFERA	LL
A_UG_U455_	RRIRQGLERA	LL
AC IN 2130	RRIRQGLERA	LL
AC_RW_92RW	SRIRQGFEAA	LQ
AC_SE_SE94	RRIRQGFERA	LL
ACD_SE_SE8	RRIRQGLERA	LL
ACG_BE_VI1	RRIRQGFERA	LL
	ARIROGLERV	LL
AD_SE_SE69	-	LL
AD_SE_SE71	RRIRQGLERA	
ADHK_NO_97	RRIRQGFERX	LL
ADK_CD_MAL	RRIRQGFERA	LL
AG_BE_VI11	RRIRQGLERA	LL
AG_NG_92NG	RRIRQGLERA	LL
AGHU_GA_VI	RRIRQGLERA	LI
AGU_CD_Z32	RRIRQGLERA	LL
AJ_BW_BW21	VRIRQGFERA	LL
B_AU_VH_AF	RRIRQGLERL	LL
B_CN_RL42_	TRIRQGLERA	LL
B_DE_D31_U	VRIRQGLERA	LL
B_DE_HAN_U	RRVRQGLERA	LL
B_FR_HXB2_	RRIRQGLERI	LL
B_GA_OYI	RRIRQGLERA	LL
B_GB_CAM1_	RRIRQGLERL	LL
B_GB_GB8_C	TRIRQGLERA	LÇ
B GB MANC	VRIRQGLERA	LL
B KR WK AF	RRIRQGLERA	LL
B_NL_3202A	VRIRQGLERA	LL
B TW TWCYS	TRIRQGLERA	LL
B_US_BC_L0	RRIRQGLERL	LL
B US DH123	TRIRQGLERA	LL
B US JRCSF	TRIRQGLERA	LL
B US MNCG	TRIRQGLERA	LL
B US P896_	TRIRQGLERA	
B_US_RF_M1	RRIRQGLERA	LL
B US SE2 K	RRIRQGLERL	
B_US_SF2_K B US WEAU1		
B US WR27	RRIRQGLERV	
B_US_YU2_M	VRIRQGLERA	LI
	RRIRQGLERA	LI
BF1_BR_93B C BR 92BR0	RRIRQGEEAA	LÇ
	TRIRQGFEAA	ΓČ
C_BW_96BW0		
C_BW_96BW1	RRIRQGFETA	LL
C_BW_96BW1	RRIRQGFEAA	LÇ
C_BW_96BW1	RRVRQGFEAA	LÇ
C_ET_ETH22	RRIRQGLEAA	LÇ
C_IN_93IN1	TRIRQGFEAA	LÇ
C_IN_93IN9	RRIRQGFEAV	LÇ
C_IN_93IN9	TRIRQGFEIA	LÇ
C_IN_94IN1	RRIRQGLEAA	LÇ
C_IN_95IN2	RRIRQGFEAA	Lζ
CRF01_AE_C	RRIRQGLERA	LI
CRF01_AE_C	RRIRQGLERA	LI
CRF01_AE_C	RRIRQGLERA	LI
CRF01_AE_T	RRIRQGLERT	LI
CRF01_AE_T	RRIRQGLERA	$_{ m LI}$
CRF01_AE_T	RRIRQGLERA	LI

```
CRF01 AE T
            RRIRQGLERA LL
CRF01 AE T
            RRIRQGLERT LL
CRF01 AE T
            RRIRQGLERA LL
CRF02 AG F
            RRIROGLERA LL
CRF02 AG F
            VRIRQGLERA LL
CRF02 AG G
            RRIRQGFERA LL
CRF02_AG_N
            RRIRQGFERA LL
CRF02_AG_S
            RRIRQGFERA LL
CRF02 AG_S
            RRIRQGLERA LQ
CRF03_AB_R
            RRIRQGAEKA LQ
CRF03_AB_R
            RRIRQGAEKA LQ
CRF04_cpx_
            RRIRQGLERA LL
CRF04_cpx_
            RRIRQGFEKA LL
CRF04_cpx_
            RRIRQGLERA LL
CRF05_DF_B
            RRIRQGLERA LL
CRF05_DF_B
            RRIRQGLERA LL
CRF06_cpx_
            RRIRQGFERA LL
CRF06_cpx_
            TRIRQGFERA LL
CRF06_cpx_
            RRIRQGAERA LI
            RRIRQGFERA LL
CRF06_cpx_
CRF11_cpx_
            RRIRQGLERA LL
            RRIRQGFERA LL
CRF11_cpx_
D CD 84ZR0
            TRIRQGLERA LL
D_CD_ELI_K
            RRIRQGLERS LL
D_CD_NDK_M
            RRIRQGLERL LL
D UG 94UG1
            VRIRQGLERA LL
F1 BE VI85
            RRIRQGAERA LL
F1 BR 93BR
            RRIRQGLERA LL
F1 FI FIN9
            RRIRQRVERA LI
F1 FR MP41
            RRIRQGLERS LL
F2 CM MP25
            RRIRQGLERA LL
F2KU BE VI
            RRIRQGFERA LL
G BE DRCBL
            RRIRQGLERA LL
G NG 92NG0
            TRIRQGLERA LL
G SE SE616
            TRIRQGLERA LL
H_BE_VI991
            RRIRQGFERA LL
H_BE_VI997
            RRIRQGLERI LL
H CF 90CF0
            RRIRQGFERS LL
J SE SE702
            RRIRQGLERA LL
J_SE_SE788
            RRIRQGLERA LL
K_CD_EQTB1
            RRIRQGFERL LL
K CM MP535
            RRIRQGLERA LL
N_CM_YBF30
            RRIRQGLERA LI
O CM_ANT70
            RRIRQGLERS LL
O CM MVP51
            RRIRQGAERI LV
O_SN_99SE_
            RRIRQGLERS LL
O_SN_99SE_
            RRIRQGLERA LL
U CD 83C
            RRIRQGFERA LL
```

Table 13. HIV Nef Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

Name:			Len:	232	Check:		Weight:	1.00
Name:	00BW0768_2	SEQ ID NO: 63	-	232	Check:	5650	Weight:	1.00
Name:	00BW0874_2	SEQ ID NO: 638	Len:	232	Check:	3483	Weight:	1.00
Name:	00BW1471_2	SEQ ID NO: 639	Len:	232	Check:		Weight:	1.00
Name:	00BW1616_2	SEQ ID NO: 640	-	232	Check:		Weight:	1.00
Name:	00BW1686_8	SEQ ID NO: 64	_	232	Check:		Weight:	1.00
Name:	00BW1759_3	SEQ ID NO: 642	Len:	232	Check:		Weight:	1.00
Name:	00BW1773_2	SEQ ID NO: 643	_	232	Check:	156	Weight:	1.00
Name:	00BW1783_5	SEQ ID NO: 644	Len:	232	Check:		Weight:	1.00
Name:	00BW1795_6	SEQ ID NO: 645	-	232	Check:	3123	Weight:	1.00
Name:	00BW1811_3	SEQ ID NO: 646	_	232	Check:		Weight:	1.00
Name:	00BW1859_5	SEQ ID NO: 64	Len:	232	Check:		Weight:	1.00
Name:	00BW1880_2	SEQ ID NO: 648	Len:	232	Check:		Weight:	1.00
Name:	00BW1921_1	SEQ ID NO: 649	en:	232	Check:		Weight:	1.00
Name:	00BW2036_1	SEQ ID NO: 650	Len:	232	Check:		Weight:	1.00
Name:	00BW2063_6	SEQ ID NO: 653	Len:	232	Check:	1020	Weight:	1.00
Name:	00BW2087_2	SEQ ID NO: 652	Len:	232	Check:	7532	Weight:	1.00
Name:	00BW2127_2	SEQ ID NO: 653	Len:	232	Check:	3425	Weight:	1.00
Name:	00BW2128_3	SEQ ID NO: 654	-	232	Check:	5136	Weight:	1.00
Name:	00BW2276_7	SEQ ID NO: 655	Len:	232	Check:	3623	Weight:	1.00
Name:	00BW3819_3	SEQ ID NO: 656	Len:	232	Check:	993	Weight:	1.00
Name:	00BW3842_8	SEQ ID NO: 65	Len:	232	Check:	6030	Weight:	1.00
Name:	00BW3871_3	SEQ ID NO: 658	Len:	232	Check:	3547	Weight:	1.00
Name:	00BW3876_9	SEQ ID NO: 659	Len:	232	Check:	1951	Weight:	1.00
Name:	00BW3886_8	SEQ ID NO: 660	_	232	Check:		Weight:	1.00
Name:	00BW3891_6	SEQ ID NO: 66	Len:	232	Check:	3655	Weight:	1.00
Name:	00BW3970_2	SEQ ID NO: 662	Len:	232	Check:	8913	Weight:	1.00
Name:	00BW5031_1	SEQ ID NO: 663	Len:	232	Check:	2223	Weight:	1.00
Name:	96BW01B21	SEQ ID NO: 664	Len:	232	Check:	2176	Weight:	1.00
Name:	96BW0407	SEQ ID NO: 665	Len:	232	Check:	5261	Weight:	1.00
Name:	96BW0502	SEQ ID NO: 666	Len:	232	Check:	333	Weight:	1.00
Name:	96BW06_J4	SEQ ID NO: 66	Len:	232	Check:	5784	Weight:	1.00
Name:	96BW11_06	SEQ ID NO: 668	Len:	232	Check:	4950	Weight:	1.00
Name:	96BW1210	SEQ ID NO: 669	Len:	232	Check:	6118	Weight:	1.00
Name:	96BW15B03	SEQ ID NO: 670	Len:	232	Check:	5089	Weight:	1.00
Name:	96BW16_26	SEQ ID NO: 67	Len:	232	Check:	3957	Weight:	1.00
Name:	96BW17A09	SEQ ID NO: 672	Len:	232	Check:	1945	Weight:	1.00
Name:	96BWMO1_5	SEQ ID NO: 673	Len:	232	Check:	5827	Weight:	1.00
Name:	96BWMO3_2	SEQ ID NO: 674	Len:	232	Check:	2303	Weight:	1.00
Name:	98BWMC12_2	SEQ ID NO: 675	Len:	232	Check:	2423	Weight:	1.00
Name:	98BWMC13_4	SEQ ID NO: 676	Len:	232	Check:	4043	Weight:	1.00
Name:	98BWMC14_a	SEQ ID NO: 67	Len:	232	Check:	3568	Weight:	1.00
Name:	98BWM014_1	SEQ ID NO: 678	Len:	232	Check:	4909	Weight:	1.00
Name:	98BWM018_d	SEQ ID NO: 679	Len:	232	Check:	3505	Weight:	1.00
Name:	98BWM036_a	SEQ ID NO: 680	Len:	232	Check:	6393	Weight:	1.00
Name:	98BWM037_d	SEQ ID NO: 68	Len:	232	Check:	1912	Weight:	1.00
Name:	99BW3932_1	SEQ ID NO: 682	Len:	232	Check:	19	Weight:	1.00
Name:	99BW4642_4	SEQ ID NO: 683	Len:	232	Check:	6848	Weight:	1.00
	99BW4745_8		Len:	232	Check:		Weight:	1.00
Name:	99BW4754_7		Len:	232	Check:		Weight:	1.00
Name:	99BWMC16_8	SEQ ID NO: 68	Len:	232	Check:		Weight:	1.00
	A2_CD_97CD		Len:	232	Check:		Weight:	1.00
Name:	A2_CY_94CY		Len:	232	Check:		Weight:	1.00
	A2D97KR		en:	232	Check:		Weight:	1.00
	A2G_CD_97C		Len:	232	Check:		Weight:	1.00
Name:	A_BY_97BL0	SEQ ID NO: 69	Len:	232	Check:	2590	Weight:	1.00

```
SEQ ID NO: 692 Len:
Name: A KE Q23
                                          232
                                               Check: 2652
                                                              Weight:
                                                                         1.00
Name: A SE SE659 SEQ ID NO: 693 Len:
                                          232
                                               Check: 9245
                                                              Weight:
                                                                         1.00
Name: A SE SE725 SEQ ID NO: 694 Len:
                                          232
                                               Check: 985
                                                              Weight:
                                                                         1.00
Name: A SE SE753 SEQ ID NO: 695 Len:
                                          232
                                               Check: 1638
                                                              Weight:
                                                                         1.00
Name: A_SE_SE853 SEQ ID NO: 696 Len:
                                          232
                                               Check: 2503
                                                              Weight:
Name: A SE SE889 SEQ ID NO: 697 Len:
                                               Check: 2327
                                                              Weight:
                                          232
                                                              Weight:
Name: A SE UGSE8 SEQ ID NO: 698 Len:
                                          232
                                               Check: 9538
Name: A UG_92UG0 SEQ ID NO: 699 Len:
                                          232
                                               Check: 2621
                                                              Weight:
Name: A UG U455 SEQ
                               700 Len:
                                          232
                                               Check: 2084
                                                              Weight:
                                                                         1.00
                       ID NO:
Name: AC IN 2130 SEQ
                       ID NO:
                               701 Len:
                                          232
                                               Check: 2406
                                                              Weight:
                                                                         1.00
Name: AC RW 92RW SEQ ID NO:
                                               Check: 3441
                               7<u>02</u> Len:
                                                                         1.00
                                          232
                                                              Weight:
Name: AC SE SE94 SEQ ID NO:
                               703 Len:
                                               Check: 3488
                                                              Weight:
                                                                         1.00
                                          232
Name: ACD_SE_SE8 SEQ ID NO: 704 Len:
                                               Check: 3016
                                          232
                                                              Weight:
                                                                         1.00
Name: ACG_BE_VI1 SEQ ID NO: 705 Len:
                                               Check: 5006
                                          232
                                                              Weight:
                                                                         1.00
Check: 3362
                                                              Weight:
                                                                         1.00
                                          232
                                               Check: 2262
                                                              Weight:
                                          232
                                                                         1.00
Name: ADHK_NO_97 SEQ ID NO: 708 Len:
                                          232
                                               Check: 8765
                                                              Weight:
                                                                         1.00
Name: ADK_CD_MAL SEQ ID NO: 709 Len:
                                          232
                                               Check: 6397
                                                              Weight:
                                                                         1.00
                                               Check: 6471
                                                              Weight:
                                                                         1.00
Name: AG_BE_VI11 SEQ ID NO: 710 Len:
                                          232
                                                              Weight:
Name: AG_NG_92NG SEQ ID NO: 711 Len:
                                          232
                                               Check: 2880
                                                                         1.00
Name: AGHU_GA_VI SEQ ID NO: 712 Len:
                                          232
                                               Check: 9053
                                                              Weight:
                                                                         1.00
Name: AGU CD Z32 SEQ ID NO: 713 Len:
                                          232
                                               Check: 523
                                                              Weight:
                                                                         1.00
Name: AJ BW BW21 SEQ ID NO: 714 Len:
                                          232
                                               Check: 3842
                                                              Weight:
                                                                         1.00
                                                              Weight:
Name: B AU VH
                   SEQ ID NO: 715 Len:
                                          232
                                               Check: 8468
                                                                         1.00
Name: B_CN_RL42 SEQ ID NO: 716 Len:
                                          232
                                               Check: 9366
                                                              Weight:
                                                                         1.00
Name: B DE D31
                   SEQ ID NO: 717 Len:
                                          232
                                               Check: 3989
                                                              Weight:
                                                                         1.00
                   SEQ ID NO: 718 Len:
                                                              Weight:
Name: B DE HAN
                                          232
                                               Check: 563
                                                                         1.00
                   SEQ ID NO: 719 Len:
                                                              Weight:
                                          232
                                               Check: 3184
                                                                         1.00
Name: B FR HXB2
                   SEQ ID NO: 720 Len:
                                          232
                                               Check: 5511
                                                              Weight:
                                                                         1.00
Name: B GA OYI
                   SEQ ID NO: 721 Len:
                                                              Weight:
Name: B GB CAM1
                                          232
                                               Check: 4779
                                                                         1.00
Name: B_GB_GB8
                   SEQ ID NO: 722 Len:
                                          232
                                               Check: 1128
                                                              Weight:
                                                                         1.00
Name: B GB MANC
                   SEQ ID NO: 723 Len:
                                          232
                                               Check: 2885
                                                              Weight:
                                                                         1.00
                   SEQ ID NO: 724 Len:
Name: B KR WK
                                          232
                                               Check: 9915
                                                              Weight:
                                                                         1.00
Name: B_NL_3202A SEQ ID NO: 725 Len:
                                          232
                                               Check: 3135
                                                              Weight:
Name: B_TW_TWCYS SEQ ID NO: 726 Len:
                                               Check: 2211
                                                              Weight:
                                          232
                                                                         1.00
Name: B_US_BC
                   SEQ ID NO: 727 Len:
                                          232
                                               Check: 3145
                                                              Weight:
                                                                         1.00
Name: B_US_DH123 SEQ ID NO: 728 Len:
                                          232
                                               Check: 7019
                                                              Weight:
                                                                         1.00
Name: B US JRCSF SEQ ID NO: 729 Len:
                                          232
                                               Check: 4099
                                                              Weight:
                                                                         1.00
Name: B_US_MNCG
                   SEQ ID NO: 730 Len:
                                          232
                                               Check: 4137
                                                              Weight:
                                                                         1.00
                   SEQ ID NO: 731 Len:
                                               Check: 4405
Name: B_US_P896
                                          232
                                                              Weight:
                                                                         1.00
                   SEQ ID NO: 732 Len:
                                               Check: 450
                                                              Weight:
                                                                         1.00
Name: B_US_RF
                                          232
                   SEQ ID NO: 733 Len:
                                               Check: 5413
                                                              Weight:
Name: B_US_SF2
                                          232
                                                                         1.00
Name: B US WEAU1 SEQ ID NO: 734 Len:
Name: B US WR27 SEQ ID NO: 735 Len:
Name: B US YU2 SEQ ID NO: 736 Len:
Name: BF1 BR 93B SEQ ID NO: 737 Len:
Name: C BR 92BR0 SEQ ID NO: 738 Len:
                                               Check: 5335
                                                              Weight:
                                                                         1.00
                                          232
                                               Check: 3720
                                          232
                                                              Weight:
                                                                         1.00
                                               Check: 9943
                                          232
                                                              Weight:
                                                                         1.00
                                               Check: 3598
                                                              Weight:
                                          232
                                                                         1.00
                                          232
                                               Check: 3908
                                                              Weight:
                                                                         1.00
                                                              Weight:
Name: C_BW_96BW0 SEQ ID NO: 739 Len:
                                          232
                                               Check: 3880
                                                                         1.00
Name: C_BW_96BW1 SEQ ID NO: 740 Len:
                                          232
                                               Check: 4542
                                                              Weight:
                                                                         1.00
Name: C_BW_96BW1 SEQ ID NO: 741 Len:
Name: C_BW_96BW1 SEQ ID NO: 742 Len:
Name: C_ET_ETH22 SEQ ID NO: 743 Len:
Name: C_IN_93IN1 SEQ ID NO: 744 Len:
Name: C_IN_93IN9 SEQ ID NO: 745 Len:
                                          232
                                               Check: 6118
                                                              Weight:
                                                                         1.00
                                          232
                                               Check: 5089
                                                              Weight:
                                                                         1.00
                                          232
                                               Check: 744
                                                              Weight:
                                                                         1.00
                                          232
                                               Check: 943
                                                              Weight:
                                                                         1.00
                                               Check: 1241
                                                              Weight:
                                          232
                                                                         1.00
                                               Check: 9885
                                                              Weight:
Name: C_IN_93IN9 SEQ ID NO: 746 Len:
                                          232
                                                                         1.00
                                                              Weight:
Name: C IN 94IN1 SEQ ID NO: 747 Len:
                                          232
                                               Check: 6448
                                                                         1.00
                                                              Weight:
Name: C_IN_95IN2 SEQ ID NO: 748 Len:
                                          232
                                               Check: 5597
                                                                         1.00
Name: CRF01_AE_C SEQ ID NO: 749 Len:
                                          232
                                               Check: 1052
                                                              Weight:
                                                                         1.00
Name: CRF01 AE C SEQ ID NO: 750 Len:
                                          232
                                                Check: 744
                                                              Weight:
                                                                         1.00
Name: CRF01_AE_C SEQ ID NO: 751 Len:
                                          232
                                               Check: 1265
                                                              Weight:
                                                                         1.00
```

```
1.00
                                              Check: 697
                                                            Weight:
Name: CRF01_AE T SEQ ID NO: 752 Len:
                                         232
Name: CRF01 AE T SEQ ID NO:
                              753 Len:
                                         232
                                              Check: 8468
                                                            Weight:
                                                                       1.00
                                              Check: 9246
                                                            Weight:
                                                                       1.00
Name: CRF01 AE T SEQ ID NO:
                              754 Len:
                                         232
                                                            Weight:
                                                                       1.00
Name: CRF01 AE T SEQ ID
                          NO:
                              755 Len:
                                         232
                                              Check: 8105
Name: CRF01 AE T SEQ ID NO:
                                         232
                                              Check: 9948
                                                            Weight:
                                                                       1.00
                              756 Len:
Name: CRF01 AE T SEQ ID NO:
                                              Check: 9460
                                                            Weight:
                                                                       1.00
                              757 Len:
                                         232
Name: CRF02 AG F SEQ ID NO:
                                              Check: 925
                                                             Weight:
                                                                       1.00
                              758 Len:
                                         232
Name: CRF02 AG_F SEQ
                                              Check: 9559
                                                            Weight:
                                                                       1.00
                               759 Len:
                                         232
                       ID NO:
Name: CRF02 AG G SEQ
                               760 Len:
                                         232
                                              Check: 399
                                                             Weight:
                                                                       1.00
                       ID NO:
Name: CRF02 AG N SEQ
                               7<u>61</u> Len:
                                         232
                                              Check: 2782
                                                             Weight:
                                                                       1.00
                       ID NO:
Name: CRF02 AG S SEQ
                                              Check: 538
                                                             Weight:
                                                                       1.00
                       ID
                          NO:
                               76<u>2</u> Len:
                                         232
Name: CRF02 AG S SEQ
                                              Check: 6700
                                                             Weight:
                                                                       1.00
                               763 Len:
                       ID
                          NO:
                                         232
Name: CRF03 AB R SEQ
                                              Check: 6784
                                                             Weight:
                               764 Len:
                                                                       1.00
                       ID NO:
                                         232
                               765
                                              Check: 3106
                                                            Weight:
Name: CRF03_AB_R SEQ
                                                                       1.00
                       ID NO:
                                  Len:
                                         232
                                              Check: 1551
                               766 Len:
                                                             Weight:
                                                                       1.00
Name: CRF04_cpx_ <u>SEQ</u>
                       ID NO:
                                         232
Name: CRF04_cpx_ <u>SEQ</u>
                                              Check: 5866
                       ID
                          NO:
                               767 Len:
                                         232
                                                            Weight:
                                                                       1.00
                       ID
                               768 Len:
                                         232
                                              Check: 7925
                                                            Weight:
                                                                       1.00
Name: CRF04_cpx_ SEQ
                          NO:
Name: CRF05_DF_B SEQ
                       ID
                          NO:
                               769 Len:
                                         232
                                              Check: 3625
                                                            Weight:
                                                                       1.00
                                               Check: 5585
                                                            Weight:
                                                                       1.00
Name: CRF05_DF_B SEQ
                       ID
                          NO:
                              770 Len:
                                         232
                          NO:
                                              Check: 3770
                                                             Weight:
                                                                       1.00
Name: CRF06_cpx_ SEQ
                       ID
                              771 Len:
                                         232
Name: CRF06_cpx_ SEQ
                      ID
                          NO:
                              772
                                  Len:
                                         232
                                              Check: 4202
                                                             Weight:
                                                                       1.00
                          NO:
                              773 Len:
                                         232
                                              Check: 5376
                                                             Weight:
                                                                       1.00
Name: CRF06_cpx_ SEQ ID
Name: CRF06_cpx_ SEQ ID
                          NO:
                              774 Len:
                                         232
                                              Check: 1869
                                                             Weight:
                                                                       1.00
                          NO:
                              775 Len:
                                              Check: 3479
                                                             Weight:
                                                                       1.00
Name: CRF11_cpx_ SEQ ID
                                         232
                                                                       1.00
Name: CRF11_cpx_ SEQ ID
                          NO:
                              77<u>6</u> Len:
                                         232
                                              Check: 3712
                                                            Weight:
                                                             Weight:
                                                                       1.00
Name: D CD 84ZR0 SEQ ID
                          NO:
                              777 Len:
                                         232
                                              Check: 1380
                                              Check: 4418
                              778 Len:
                                                             Weight:
                                                                       1.00
Name: D CD ELI
                   SEQ ID
                          NO:
                                         232
                                                             Weight:
                                                                       1.00
                   SEQ ID NO: 779 Len:
                                         232
                                              Check: 4588
Name: D CD NDK
Name: D_UG_94UG1 SEQ_ID_NO:
                              780 Len:
                                              Check: 2178
                                                            Weight:
                                                                       1.00
                                         232
                              781 Len:
                                                             Weight:
                                                                       1.00
Name: F1 BE VI85 SEQ ID
                          NO:
                                         232
                                              Check: 4350
                                                                       1.00
Name: F1 BR 93BR SEQ ID
                          NO:
                              782 Len:
                                         232
                                              Check: 7703
                                                             Weight:
Name: F1 FI FIN9 SEQ ID
                          NO:
                              783 Len:
                                         232
                                              Check: 5036
                                                             Weight:
                                                                       1.00
Name: F1 FR MP41 SEQ ID
                          NO:
                              784 Len:
                                         232
                                              Check: 84
                                                             Weight:
                                                                       1.00
Name: F2 CM MP25 SEQ ID
                              785 Len:
                                         232
                                              Check: 2622
                                                             Weight:
                                                                       1.00
                          NO:
Name: F2KU BE VI SEQ ID
                              786 Len:
                                         232
                                              Check: 2193
                                                             Weight:
                                                                       1.00
                          NO:
                                              Check: 2548
                                                             Weight:
                                                                       1.00
Name: G BE DRCBL SEQ ID
                          NO:
                              787
                                  Len:
                                         232
                                                             Weight:
Name: G_NG_92NG0 SEQ ID
                          NO:
                              788
                                  Len:
                                         232
                                              Check: 3608
                                                                       1.00
Name: G SE_SE616 SEQ
                       ID
                          NO:
                              789
                                  Len:
                                         232
                                              Check: 2716
                                                             Weight:
                                                                       1.00
Name: H BE VI991 SEQ
                       ID
                          NO:
                              790 Len:
                                         232
                                              Check: 1561
                                                             Weight:
                                                                       1.00
Name: H BE_VI997 SEQ
                              791 Len:
                                              Check: 663
                                                             Weight:
                                                                       1.00
                       ID
                          NO:
                                         232
                          NO:
Name: H CF 90CF0 SEQ
                       ID
                               792
                                              Check: 1804
                                                            Weight:
                                                                       1.00
                                  Len:
                                         232
Name: J SE SE702 SEQ
                       ID
                               793
                                              Check: 1615
                                                             Weight:
                                                                       1.00
                          NO:
                                         232
                                  Len:
Name: J SE SE788 SEQ
                              794
                                              Check: 1704
                                                            Weight:
                                                                       1.00
                       ID
                          NO:
                                  Len:
                                         232
                              795
Name: K CD EQTB1 SEQ
                       ID
                          NO:
                                  Len:
                                         232
                                              Check: 4783
                                                             Weight:
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Name: K CM MP535 SEQ
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                                  Len:
                                         232
                                               Check: 2033
                                                             Weight:
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                                                                       1.00
                              798 Len:
Name: O CM ANT70 SEQ
                       ID
                          NO:
                                         232
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                              799
Name: O CM MVP51 SEQ
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                                  Len:
                                         232
                                               Check: 5835
                                                             Weight:
                                                                       1.00
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                       ID
                          NO:
                              800 Len:
                                         232
                                               Check: 8625
                                                             Weight:
                                                                       1.00
Name: O_SN_MP130 SEQ ID NO:
                              801 Len:
                                         232
                                               Check: 8793
                                                             Weight:
                                                                       1.00
Name: U_CD___83C SEQ ID NO: 802 Len:
                                         232
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                                                             Weight:
                                                                        1.00
SEQ ID NO
                                                                                50
            00BW0762 1
                        MGGKWSKSS. IVGWPAVRER IR....RTDP ..........AAEGVG
636
            00BW0768 2
                        MGGKWSKSSI V.GWPEVRER IRR..TEP.. .....AAEGVG
637
            00BW0874 2
                        MGGKWSKSS. LTGWPAVRER IR....RTEP ............AAEGVG
638
                        MGGKWSKSS. IVGWPAVKER IRR..TNPR. ..... .TERAAVGVG
            00BW1471 2
639
            00BW1616 2
                        MGNKWSKSS. IVGWPAVRDR MRR..AEP.......AAEGVG
640
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641	00BW1686_8	MGGKWSKRS.	KYDMDYNDEK	T.D TTED		AAEGVG
642	00BW1759 3			IRRTRPAR		
643	00BW1773 2			IRRTEP		
644	00BW1783 5			IRRTNPAA		
645	00BW1795 6			MRR		
646	00BW1811 3			MRR		
647	00BW1859 5			MRRTRPAA		
648	00BW1880 2			IRTTAP		
649	_	MGGKWSKSS.				
650	00BW2036 1			IRR		
651	00BW2063 6			MRKAEP		
652	00BW2087 2			IRRT		
653	_ 00BW2127 2			IRRTEP		
654	00BW2128 3			IRRAEP		
655	_ 00BW2276 7			MRRATPAA		
656	00BW3819 3			MRRARPAV		
657	00BW3842 8			MRR		
658	00BW3871 3			LRKTEP		
659	00BW3876 9					AAEGV G
660	00BW3886 8			MKRTEP		
661		MGGKWSKSS.				
662	-	MGSKWSKRS.				
663	00BW5031 1			IRRTDP		
664	96BW01B21			IRRTEP		
665	96BW0407			MRRAEP		
666	96BW0502			MRRTRPAV		
667	96BW06_J4			IRRTDP		
668	_ 96BW11 06	MGGKWSKSSI	I.GWPAIRER	IRRTEPAA	ERV	GAAAEGVG
669	96BW1210			IRRTEPAT		
 670	96BW15B03	MGGKWSKSS.	IVGWPAVRER	IRR		. TEPAAEGVG
	96BW16 26	MGGKWSK	WPAVRER	MRRTR		VG
672	_ 96BW17A09	MGXKWSKRS.	IVGWPNVRER	IRRTNPLT	ER	EAERAAVGVG
673	96BWM01_5	MGSKWSKSSI	I.GWPAVRER	IRKTEPRK		. TEPAAEGVG
 674	96BWMO3_2	MGGKWSKSS.	IVGWPAVRER	MRRTRPGA	AE	gvg
675	98BWMC12_2	MGSKWSKSS.	IIGWPAVRER	MRRTEP		AAEGVG
676	98BWMC13_4	MGGKWSKSS.	IIGWPAVRER	MRR		. TEPAAEGVG
	98BWMC14_a	MGGKWSKSS.	LVGWPDVRER	IRKPRP	KP	AAEGVG
678	98BWM014_1	MGSKLSKSK.	IVGWPAIRER	LR		RTEPAAEGVG
679	98BWM018_d	MGGKWSKSS.	IVGWPAVRER	IRQTDPRE	$\mathtt{RI}\ldots\ldots\mathtt{R}$	QTEPAAEGVG
680	98BWMO36_a	MGGKWSKSSI	V.GWPAVRER	IRRTEPRR		.AEPAAEGVG
681	98BWM037_d	MGGKWSKSS.	IVGWPEVRER	LRRTAP		AAEGVG
682	99BW3932_1	MGGKWSKRKI	V.QWPTVRER	LRRTEP		AEGVG
683	99BW4642_4	MGGKWSKSS.	IVGWPAVRER	IRRTQPAA	EG	vg
<u>684</u>	99BW4745_8	MGSKLSKSC.	TAGWPTVRER	IRQAEP		AAEGVG
<u>685</u>	99BW4754_7			MRR		
<u>686</u>	99BWMC16_8			IRRTEPAV		
<u>687</u>	A2_CD_97CD	MGGKWSKRT.	IVGWPEIRER	MRRTPPAA	EGVR	PTPPAAEGVG

688	A2 CY 94CY	MGGKWSKRS.	IPGWPAIRER	MRRTPPTAQR	TE	AVSPAAPGVG
689	A2D 97KR			MRRTPPAAER		
690	A2G CD_97C			IRQTPP.		
691	A_BY_97BL0			IRRAPAP		
692	A KE_Q23			MRRAPP		
693	A SE SE659			MRRAPS		
694	A_SE_SE725	MGSKWSKSS.		LRQTLAAARG		
695	 A_SE_SE753	MGGRWSKSR.		IRRAPP		
696	A SE SE853			IRQT		
697	A SE SE889	MGGKWSKSS.	IVGWPKVRER	MARTPP		AAKGVG
698	A SE UGSE8	MGNKWSK	GWPEVRER	IRQARAPAHT		PAPTAATGVG
699	A_UG 92UG0	MGNKWSKSC.	IVGWPEVRER	IRQTPTAARE	RTR	QAPTAAKGVG
700	A UG U455	MGGKWSKKS.	RVEWPEVRKR	MRETPA		AAKGVG
701	AC IN 2130	MGGKWPKSS.	VVGWPEVRER	IRRTPA		AAPGVG
702	AC RW 92RW	MGSKWSKCSP	V.GWPAVRER	LRQTEP		AAEGVG
703	AC_SE_SE94	MGGKWSKSS.	IIGWPQIRER	IRRTPP		AATGVG
704	ACD_SE_SE8	MGGKWLKSSI	V.GWPAVRER	IRRTEP		AAEGVG
705	ACG_BE_VI1	MGGKWSKRS.	KVEWPQVRER	MRQTPIAA	EA EG	AAAEGVG
706	AD_SE_SE69	MGGKWSKSS.	IVGWPAVRER	IKRT		DPAAEGVG
707	AD_SE_SE71	MGGKWSKSS.	IVGWPEVRER	MRRARAP		SAAPGVG
708	ADHK_NO_97	MGGKWSKSS.	IVGWPAIRER	MRRAEP		AAEGVG
709	ADK_CD_MAL	MGGKWSKSS.	IVGWPKIRER	IRRTPPTETG		VGAVSQD
710	AG_BE_VI11	MGGKWSKSS.	PVGWSRVRER	MRRTPPAA	EG	AAAEGVG
711	AG_NG_92NG	IGGKWSKSS.	IVGWPAVRER	IRQTP		PAEGVG
712	AGHU_GA_VI	MGGEWSRSS.	IVGWSTIRER	MRRAEP		AAAGVG
713	AGU_CD_Z32	MGNKWSKG	WPAVRER	IRQTPPAP	P	AAEGVG
714	AJ_BW_BW21	MGSNWSKS.S	IIGWPQVRER	MKRAP	${\tt A}\dots {\tt P}$	AAEGVG
715	B_AU_VH	MGGKGSKRI.	RSEWPTVRER	IIQAEPAA	AG	VG
716	B_CN_RL42	MGGKWSKHS.	MFGWPSVRER	MKRAEPAA	DG	VG
<u>717</u>	B_DE_D31	MGGKWSKSS.	VVGWPAIRER	$\texttt{MK}.\dots\dots$		RAEPAAEGVG
718	B_DE_HAN			MKQAEP		
<u>719</u>	B_FR_HXB2	MGGKWSKSS.	VIGWPTVRER	MR		RAEPAADRVG
720	B_GA_OYI	MGGKWSKCS.	MKGWPTIRER	MKRAELQP	PE	PAAEGVG
721	B_GB_CAM1			MQRAEP		
722	B_GB_GB8			MQQAEP		
723	B_GB_MANC			MKQVDPAE		
724	B_KR_WK			MRRAEPAA		
<u>725</u>	B_NL_3202A			MK		
726	B_TW_TWCYS			IRQAEPA.		
727	B_US_BC			MR		
728	B_US_DH123			MRRAEPAA		
729	B_US_JRCSF			MRRAEPAT		
730	B_US_MNCG			MRRAEP		
<u>731</u>	B_US_P896			MRRAEPA		
<u>732</u>	B_US_RF			MQKAEPAA		
<u>733</u>	B_US_SF2			MRRAEP		
734	B_US_WEAU1	MGGIWSKRS.	GSGWPAIRER	MKRAEPAA	EG	· · · · · · · · VG

135	725	B US WR27	MCCKWCKDC	VGGWDATPEP	ΜΥ	 RAEPAAEGVG
### BP1_BR_93B MGSKWSKSS IVGWPAIRER LRQ	735 736					
738 C_BR_92BRO MGNKWSKCST V.GRPAIRER MRR. AP. AAEGVG 739 C_BW_95BWO MGGKWSKSSI V.GWPAVER MRR. TEPP. AAEGVG 740 C_BW_95BW1 MGGKWSKSKI V.GWPAVRER MRR. TEPPA AAEGVG 741 C_BW_95BW1 MGGKWSKSKI V.GWPAVRER IRR. TEPAT .EPAAEGVG 742 C_BW_95BW1 MGGKWSKSSI V.GWPAIRER IRR. AAP. .AAEGVG 743 C_ET_ETI22 MGGTMSKCSP V.GWPAIRER IRR. AAP. .AAEGVG 744 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. AEP. .AAEGVG 745 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. TEP. .AAEGVG 746 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. TEP. .AAEGVG 747 C_IN_94IN1 MGGKWSKCSI V.GWPAIRER MRR. TEP. .AAEGVG 749 C_IN_95IN2 MGGKWSKCSI V.GWPAIRER MRR. TEP. .AAEGVG 750 CRF01_AB_C MGGKWSKSCI V.GWPAIRER MRR. TEP. .AAEGVG 751 CRF01_AB_C MGGKWSKS. IVGWPQVRE IRC. TPVAT .EGVG 752 CRF01_AB_C MGKWSKS. IVGWPQVRE IRC. TPVAT .EGVG 753 CRF01_AB_T						
739 C_BW_968W1 MGGKWSKSSI V.GWPAVRER MRR. TEP. .AAEGVG 740 C_BW_968W1 MGGKWSKSSI I.EWPTITOR MRR. TEPAA EG V.GAAABCVG 741 C_BW_968W1 MGKWSKSS. IVGWPAVRER IRR. TEPAT EPAABGVG 742 C_BW_968W1 MGGKWSKSS. IVGWPAVRER IRR. TEPAABGVG 743 C_ET_ETH22 MGGTMSKCSP V.GWPAIRER MRR. AAP AAEGVG 744 C_IN_93IN9 MGGKWSKCSI V.GWPAIRER MRR. AAP AAEGVG 745 C_IN_93IN9 MGGKWSKCSI V.GWPAIRER MRR. TOP AAEGVG 746 C_IN_93IN9 MGGKWSKCSI V.GWPAIRER MRR. TOP AAEGVG 747 C_IN_94IN1 MGGKWSKCSI V.GWPAIRER MRR. TOP AAEGVG 747 C_IN_94IN1 MGGKWSKCSI V.GWPAIRER MRR. TOP AAEGVG 749 CRP01_AE_C MGGKWSKCSI V.GWPAIRER MRR. TOP AAEGVG 750 CRF01_AE_C MGGKWSKS. IVGWPQVRER IRR. TPAA BCVG 751 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRR. TPAA BCVG 752 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRR. TPAA BCVG 753 <td< td=""><td></td><td></td><td></td><td></td><td></td><td></td></td<>						
740 C_BW_96BW1 MGGKWSKRSK I.EWPTIRDR MRR. TEPAA EG. V GAAABGVG 741 C_BW_96BW1 MGNKWSKS. WPAVRDR IRR. TEPAT EPAABGVG 742 C_BW_96BW1 MGKWSKSS. IVGWPAVRER IRR. TEPAABGVG 743 C_ET_ETH22 MGGTMSKCSP V.GWPAIRER IRR. AAEGVG 744 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. AEF. AAEGVG 745 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. TEP. AAEGVG 746 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. TEP. AAEGVG 747 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. TEP. AAEGVG 748 C_IN_95IN2 MGGKWSKCSI V.GWPAIRER MRR. TEP. AAEGVG 749 CRF01_AE_C MGGKWSKSCI V.GWPDIRER MRR. TEP. AAEGVG 750 CRF01_AE_C MGGKWSKS. IVGWPQVRER IRQ. TPVAA EGVG 751 CRF01_AE_C MGKWSKS. IVGWPQVRER IRQ. TPPAA EGVG 752 CRF01_AE_T MGCKWSKS. IVGWPQVRER IRQ. TPPAA EGVG 753 CRF01_AE_T MGCKWSKS.						
741 C_BW_96BW1 MGNKWSKG. .WPAVRDR IRR. TEPAT .EPAABGVG 742 C_BW_96BW1 MGGKWSKSS. IVGWPAVRER IRR. .TEPAALGVG 743 C_ET_ETH22 MGGKWSKCSI V.GWPAIRER IRR. .AAPGVG 744 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. AEP. .AABGVG 745 C_IN_93IN9 MGGKWSKCSI V.GWPAIRER MRR. TEP. .AABGVG 746 C_IN_93IN1 MGGKWSKCSI V.GWPAVRER MRR. TEP. .AABGVG 747 C_IN_94IN1 MGGKWSKCSI V.GWPAVRER MRR. TEP. .AABGVG 748 C_IN_95IN2 MGGKWSKCSI V.GWPAVRER MRR. TEP. .AABGVG 749 CRF01_AE_C MGGKWSKCSI V.GWPAVRER IRR. TEP. .AABGVG 750 CRF01_AE_C MGGKWSKS. IVGWPQVRER IRR. TEPA. .ABGVG 751 CRF01_AE_C MGKWSKS. IVGWPQVRER IRR. TEPA. .BGVG 752 CRF01_AE_T MGGKWSKS. IVGWPQVREK IRQ. TPPAA .BGVG 753 CRF01_AE_T MGGKWSKS. IVGWPQVREK IRQ. TPPAA .BGVG 754 CRF01_AE_T MGAKWSKS. IVGWPQVRER IRQ. TPPAA .BGVG 755 <		- -				
742 C_BW_96BW1 MGGKWSKSS. IVGWPAVRER IRR. TEPAAEGYG 743 C_ET_ETH22 MGGTMSKCSP V. GWPAIRER IRR. AAP. AABGYG 744 C_IN_93IN9 MGGKWSKCSI V. GWPAIRER MRR. AAP. AABGYG 745 C_IN_93IN9 MGGKWSKCSI V. GWPAIRER MRR. TOP. AABGYG 746 C_IN_95IN1 MGGKWSKCSI V. GWPAIRER MRR. TOP. AABGYG 747 C_IN_95IN2 MGGKWSKCSI V. GWPAIRER MRR. TOP. AABGYG 748 C_IN_95IN2 MGGKWSKCSI V. GWPDIRER MRR. TOP. AABGYG 749 CRF01_AE_C MGGKWSKCSI V. GWPDIRER MRR. TEP. AABGYG 750 CRF01_AE_C MGGKWSKS. IVGWPQVRER IRQ. TPVAE E. R QFPAAABGYG 751 CRF01_AE_C MGGKWSKS. IVGWPQVRER IRQ. TPVAE E. R QFPAAAABGYG 752 CRF01_AE_T MGGKWSKS. IVGWPQVREK IKQ. TPPAA BGYG 753 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRQ. TPPAA BGYG 754 CRF01_AE_T						
743 C_ET_ETH22 MGGTMSKCSP V.GWPAIRER IRR. AAP. AAEGVG 744 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. ABP. AAEGVG 745 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. TPP. AAEGVG 746 C_IN_93IN1 MGGKWSKCSI V.GWPAIRER MRR. TEP. AAEGVG 747 C_IN_94IN1 MGGKWSKCSI V.GWPEIRER MRR. TEP. AAAGVG 748 C_IN_95IN2 MGGKWSKCSI V.GWPEIRER MRR. TEP. AAAEGVG 750 CRF01_AE_C MGGKWSKCSI V.GWPQVRER IRR. TPAAA .EGVG 751 CRF01_AE_C MGKWSKS. IVGWPQVRER IRR. TPAAA .EGVG 752 CRF01_AE_C MGKWSKS. IVGWPQVRER IRQ. TPVAT .EGVG 753 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRQ. TPVAA .EGVG 754 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRQ. TPVAA .EGVG 755 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRQ. TPVAA .EGVG 756 CRF01_AE_T MGKWSKS. IVGWPQVRER IRQ. TPVAA .EGVG 757 CRF01_AE_T MGKWSKS. IVGWPQVRER IRQ. TPVAA .EGVG 757 CRF01_AE_T MGKWSKSS.		– –				
Total						
Table		- -				
746 C_IN_93IN9 MGGKWSKCSI V.GWPAVRER MRR.TEP. AAEGVG 747 C_IN_94IN1 MGGKWSKCSI V.GWPEIRER MRR.TOP. AADGVG 748 C_IN_95IN2 MGGKWSKCSI V.GWPDIRER MRR.TEP. AAAGVG 749 CRF01_AE_C MGGKWSKCSI V.GWPDIRER MRR.TEP. AAAGVG 750 CRF01_AE_C MGGKWSKSC. IVGWPQVRER IRQ.TPVAE E. R QTPAAAEGVG 751 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRQ.TPVAE E. R QTPAAAEGVG 752 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRQ.TPVAA EGVG 753 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRQ.TPVAA EGVG 754 CRF01_AE_T MGGKWSKS. IVGWPQVRER IRQ.TPVAA EGVG 755 CRF01_AE_T MGSKWSKS. IVGWPQVRER IRQ.TPVAA EGVG 756 CRF01_AE_T MGSKWSKS. IVGWPQVRER IRQ.TPVAA EGVG 757 CRF01_AE_T MGSKWSKS. IVGWPQVRER IRQ.TPVAA EGVG 759 CRF02_AG_F MGGKWSKS. IVGWPQVRER IRQ.TPVA AATGVG 760 CRF02_AG_G MGGKWSKSS. IVGWPQVRER IR.QTPP. AARGVG 761 CRF02_AG_S MGGKWSKS						
747 C_IN_94IN1 MGGKWSKCSI V.GWPEIRER MRR. TQP. AADGVG 748 C_IN_95IN2 MGGKWSKN.R IVGWPQVRER IRR. TFPA. AAEGVG 750 CRF01_AE_C MGGKWSKN.R IVGWPQVRER IRR. TPAAA EGVG 751 CRF01_AE_C MGGKWSKSWPQIRER IRQ. TPVAT EGVG 752 CRF01_AE_T MGGKWSKSWPQIRER IRQ. TPVAT EGVG 753 CRF01_AE_T MGGKWSKS.S IVGWPQVREK IKQ. TPPAA EGVG 754 CRF01_AE_T MGGKWSKS.S IVGWPQVRER IKQ. TPPAA EGVG 755 CRF01_AE_T MGGKWSKS.S IVGWPQVRER IKQ. TPPAA EGVG 756 CRF01_AE_T MGGKWSKS.S IVGWPQVRER IKQ. TPPAA EGVG 757 CRF01_AE_T MGGKWSKS.S IVGWPQVRER IKQ. TPPAA EGVG 758 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IKQ. TPPAA EGVG 759 CRF01_AE_T MGGKWSKSS. IVGWPQVRER IKQ. TPPAA EGVG 759 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IRQ. TPPAA AARGVG 761 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IRQ. TPPAA AARGVG 762 <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>						
748 C_IN_95IN2 MGGKWSKCSI V.GWPDIRER MRR.TEP. AAAEGVG 749 CRF01_AE_C MGGKWSKN.R. IVGWPQVRER IRR.THAAA BGVG 750 CRF01_AE_C MGGKWSKSC. IVGWPQVRER IRQ.TPVAE R. QTPAAAEGVG 751 CRF01_AE_C MGKWSKSWPQIRER IRQ.TPVAT BGVG 752 CRF01_AE_T MGGKWSKS.S. IVGWPQVRER IKQ.TPPAA BGVG 753 CRF01_AE_T MGGKWSKS.S. IVGWPQVRER IKQ.TPPAA BGVG 754 CRF01_AE_T MGGKWSKS.S. IVGWPQVRER IKQ.TPPAA BGVG 755 CRF01_AE_T MGAKWSKS.S. IVGWPQVRER IKQ.TPPAA BGVG 756 CRF01_AE_T MGAKWSKS.S. IVGWPQVRER IKQ.TPPAA BGVG 757 CRF01_AE_T MGAKWSKS. IVGWPQVRER IKQ.TPPAA BGVG 758 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IKQ.TPPAA BGVG 759 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IRQ.TPPA AATGVG 750 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IRQ.TPPA AATGVG 761 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IRQ.QTPT AATGVG 762 CRF		- -				
749 CRF01_AE_C MGGKWSKN.R IVGWPQVRER IRR. TPAAA						
750 CRF01_AE_C MGGKWSKSC. IVGWPQVRER IRQ. TPVAE E. R QTPAAAEGVG 751 CRF01_AE_C MGNKWSKS. WPQ1RER IRQ. TPVAT EGVG 752 CRF01_AE_T MGGKWSKS.S IVGWPQVREK IKQ. TPPAA EGVG 753 CRF01_AE_T MGGKWSKS.S IVGWPQVREK IKQ. TPPAA EGVG 754 CRF01_AE_T MGGKWSKS.S IVGWPQVRER IKQ. TPPAA EGVG 755 CRF01_AE_T MGAKWSKSS. IVGWPQVRER IKQ. TPPAA EGVG 756 CRF01_AE_T MGAKWSKSS. IVGWPQVRER IKQ. TPPAA EGVG 757 CRF01_AE_T MGAKWSKSS. IVGWPQVRER IKQ. TPPAA EGVG 758 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IRQ. TPPA AATGVG 759 CRF02_AG_F MGGKWSKSS. IVGWPQVRER IRQTPP. AATGVG 760 CRF02_AG_S MGGKWSKSS. IVGWPQVRER IRQTPT. AATGVG 761 CRF02_AG_S		_ _				
751 CRF01_AE_C MGNKWSKS. WPQIRER IRQ. TPVAT EGVG 752 CRF01_AE_T MGGKWSKS.S. IVGWPQVREK IKQ. TPPAA EGVG 753 CRF01_AE_T MGGKWSKS.S. IVGWPQVREK IKQ. TPPAA EGVG 754 CRF01_AE_T MGGKWSKS.S. IVGWPQVREK IKQ. TPPAA EGVG 755 CRF01_AE_T MGSKWSKS.S. IVGWPQVREK IKQ. TPPAA EGVG 756 CRF01_AE_T MGSKWSKS.S. IVGWPQVREK IKQ. TPPAA EGVG 757 CRF01_AE_T MGSKWSKS.S. IVGWPVRER IKQ. TPPAA EGVG 759 CRF02_AG_F MGGKWSKSS. IVGWPVRER IKQ. TPPAA EGVG 759 CRF02_AG_G MGGKWSKSS. IVGWPVRER IKQ. TPPA AATGVG 750 CRF02_AG_G MGGKWSKSS. IVGWPVRER IR. QTPT. AATGVG 761 CRF02_AG_G MGGKWSKSS. IVGWPVRER IR. QTPT. AATGVG 762 CRF02_AG_S MGGKWSKSS.		– –				
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754 CRF01_AE_T MGGKWSKS.S IVGWPQVRER IKQ. TPPAA EGVG 755 CRF01_AE_T MGAKWSKRG WPQVRER IRQ. TPPAA EGVG 756 CRF01_AE_T MGSKWSKS.S IVGWPQVRER IRQ. TPPAA EGVG 757 CRF01_AE_T MGSKWSKS.S IVGWPVRER IKQ. TPPAA GVG 758 CRF02_AG_F MGGKWSKSS IVGWPKVRER IRQTPP. AATGVG 759 CRF02_AG_G MGGKWSKSS LVGWPKVRER IIQTPP. AATGVG 760 CRF02_AG_G MGGKWSKSS LVGWPQVRER IRQTPT. AAKGVG 761 CRF02_AG_S MGGKWSKSS LVGWPQVRER IRQTPT. AARGVG 762 CRF02_AG_S MGGKWSKSS LVGWPQVRER IRQTPT. AARGVG 764 CRF02_AG_S MGGKWSKSS LVGWPQVRER IRRQTPT. AARGVG 764 CRF03_AB_R MGGKWSKSS LVGWPQVRER IRRAPAP. AARGVG 765 CRF03_AB_R MGGKWSKSS						
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762 CRF02_AG_S MGGKWSKSS. IVGWPQIRDR IRQTPP. AARGVG 763 CRF02_AG_S MGGKWSKSS. LVGWPQVRER IRRTQPTPS. AAIGVG 764 CRF03_AB_R MGGKWSKSS. IVGWPQVRER IRRAPAP. AARGVG 765 CRF03_AB_R MGGKWSKSS. IVGWPQIRER IRRAPAP. AARGVG 766 CRF04_cpx_ MGGKWSKSS. IVGWPQIRER IRRAPAP. AARGVG 767 CRF04_cpx_ MGGKWSKSS. LVGWPAIRER MRR. ARAEP AA QAEPAAAGVG 768 CRF04_cpx_ MGGKWSKSS. LVGWPAIRER MRR. ARAEP AA QAEPAAAGVG 769 CRF05_DF_B MGGKWSKSS. VVGWPAIRER MRR. ARAEP A RAEPAAVGVG 770 CRF05_DF_B MGGKWSKSS. VVGWPAIRER MRR. TPPAA GAAAEGVG 771 CRF06_cpx_ MGNKWSKS. IVGWPAIRER MRR. TPPTE R. AAEGVG 773 CRF06_cpx_ MGGKWSKS. IVGWPAURER IRQ. TPPTE G. AAEGVG 774 CRF06_cpx_						
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767 CRF04_cpx_ MGGKWSKSS. LVGWPAIRER MRR. ARAEP AA QAEPAAAGVG 768 CRF04_cpx_ MGNKWSKS. WPAVRER MRR. ARAEPA A RAEPAAVGVG 769 CRF05_DF_B MGGKWSKSS. VVGWPAIREK MRR. TP. PAAEGVG 770 CRF05_DF_B MGGKWSKNR. IVGWPAIRER MRR. TPPAA GAAAEGVG 771 CRF06_cpx_ MGNKWSK. GWSQVRER MRR. TPPTE R. AAEGVG 772 CRF06_cpx_ MGGKWSKS.S IVGWPQVRER IRQ. TPPTE G. AAEGVG 773 CRF06_cpx_ MGGKWSKS.S IVGWPQVRER IRQ. TPPTE G. AAEGVG 774 CRF06_cpx_ MGGKWSKS.S IVGWPEIRER MRQ. TPPAA R QTPPAAEGVG 775 CRF11_cpx_ MGGKWSKS.S IVGWPEIRER LRR.						
768 CRF04_cpx_ MGNKWSKS. WPAVRER MRR. ARAEP A RAEPAAVGVG 769 CRF05_DF_B MGGKWSKSS. VVGWPAIREK MRR. TP. PAAEGVG 770 CRF05_DF_B MGGKWSKNR. IVGWPAIRER MRR. TPPAA GAAAEGVG 771 CRF06_cpx_ MGNKWSK. GWSQVRER MRR. TPPTE R. AAEGVG 772 CRF06_cpx_ MGSKWSKS.S IVGWPQVRER IRQ. TPPTE G. AAKGVG 773 CRF06_cpx_ MGGKWSKS.S LVGWPQVRER IRQ. TPPTE G. AAEGVG 774 CRF06_cpx_ MGGKWSKS.S IVGWPKVRER MRQ. TPPAA E. R QTPPAAEGVG 775 CRF11_cpx_ MGGKWSKS.S IVGWPEIRER LRR. T PPTAAAEGVG 776 CRF11_cpx_ MGGKWSKS.S IVGWPAIRER IRK. TDPRE RR. RPEPAADGVG 778 D_CD_84ZRO MGGKWSKSS. IVGWPAIRER IRK. T. NPAADGVG 779 D_CD_NDK MGGKWSKSS. LVGWPAIRER IRK. T. DPAADGVG 780 D_UG_94UG1 MGGKWSKSS. IVGWPAVRER MRR. T. EPAAEGVG		<u>-</u>				
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770CRF05_DF_BMGGKWSKNR.IVGWPAIRER MRR.TPPAA						
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779 D_CD_NDK MGGKWSKSS. LVGWPAIRER IRKT		- -				
780 D_UG_94UG1 MGGKWSKSS. IVGWPAVRER MRRT EPAAEGVG						
	 _					
781 F1_BE_V185 MGGKWSKSS. IVGWPAVGER MRQTP						
	<u>781</u>	F1_BE_V185	MGGKWSKSS.	IVGWPAVGER	MRQTP	 TAAEGVG

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F1_BR_93BR MGGKWSKSS. IVGWPAIRER MRR..TPPT. ...... ..PPAAEGVG
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          F1 FI FIN9
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          F1 FR MP41
          F2 CM MP25
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785
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786
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          G_BE_DRCBL MGNKWSKRK. VAGWPEVRER LR...QHPA. ......AAEGVG
787
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788
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789
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790
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          K CM MP535
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798
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          O_CM_MVP51
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          O SN MP129
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A BY 97BLO PVSQDXDKHG AVTSSNTAAN NADCAXLEAQ X...EXEVGF PVRPQVPLRP
  A KE Q23 AVSQDLDKHG AVTSKNINH. .PSYAWLEAQ E...DEDVGF PVRPQVPLRP
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A SE SE753
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A SE SE853
A SE SE889 AVSQDLDKHG AVTSSNINH. .PSCAWVEAQ E...EEEVGF PVRPQVPLRP
A SE UGSE8 AVSODLEKHG AITSSNINH. . PSCTWLEAQ AQE.DEEVGF PVRPQVPLRP
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AC RW 92RW
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   B_KR_WK AASRDLEQRG AITTSNTASN NAACAWQEAQ EEE...EVGF PVRPQVPLRP
B NL 3202A AVSRDLEKHG AITSSNTAAT NADCAWLEAQ EDE...EVGF PVKPQVPLRP
B_TW_TWCYS AVSRDLEKHG AITSSNTAAT NADCAWLEAQ EEE...EVGF PVRPQVPLRP
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B_US_BC AVSRDLEKHG AITSSNTAAN NADCAWLEAQ EEE...EVGF PVRPQVPLRP
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99BW4745_8 DREVLRWKFD SHLARRHMAR E.LHPEFYKD C.
99BW4754_7
            HKEVLKWKFD SHLARRHMAR E.LHPEFYKD C.
99BWMC16_8 DREVLKWQFD SSLARRHMAR E.LHPEYYKD C.
A2_CD_97CD EREVLKWKFD SRLALRHLAR E.QHPEFYKD C.
A2_CY_94CY EREVLRWEFD RSLARRHRAR E.LHPEYYKD C.
A2D___97KR EREVLKWVFD SHLALVHKAR E.LHPEFYKD C.
A2G_CD_97C DKQVLGWRFD SSLARRHIAR E.KHPEYYKD C.
A_BY_97BL0 EKEVLMWKFD SRLALKHRAR E.LHPEFYKD C.
  A_KE_Q23 EREVLKWKFD SRLALKHRAR E.LHPEWYKD C.
A_SE_SE659 EKEVLKWKFD SRLALKHLAC E.KHPEFYKD C.
A_SE_SE725 EKETLRWRFD SRLALRHRAQ E.MHPEFYKD C.
A_SE_SE753 EREVLKWKFD SRLALKHRAQ E.LHPEFYKD C.
A_SE_SE853 ERETLMWKFD SKLALKHRAH E.LHPEYFKN C.
A_SE_SE889 ERETLMWKFD SRLALTHRAR E.LHPEFYKD C.
A_SE_UGSE8 ERETLMWKFD PHLAFKHRAF E.LHPEYYKN ..
A UG 92UG0 EKETLRWKFD SSLARVHKAR E.LHPEFYKD C.
```

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A UG U455
            EKEVLMWKFD STLALKHRAY E.LHPEFYKD
AC IN 2130
            YGEVLQWKFD SHLAYKHQAR E.RHPEFYKD C.
AC RW 92RW
            DREVLKWKFD SHLAHRHMAR E.LHPEYYKD C.
AC SE SE94
            ERETLVWRFD SRLALKHLAR E.KHPEFYKD C.
ACD SE SE8
            DKEVLRWKFD SQLARRHMAR E.MHPEYYKD C.
ACG BE VI1
            DREVLVWRFD SRLALKHIAK E.KHPEYFKD C.
AD SE SE69
            EREVLMWRFN SRLAFEHKAH Q.LHPEYYKD C.
AD_SE_SE71
            EKEVLKWQFD SRLALKHLAR E.KHPEFYKD C.
ADHK NO_97
            EXEVLMWRFD SRLAFKHRAR E.LHPEFYKD C.
ADK CD MAL
            EREVLKWKFD SSLALRHRAR E.QHPEYYKD C.
AG BE VI11
            EREVLVWKFD SMLAFKHRAR E.LHPEYYKD C.
AG NG_92NG
            DREVLVWRFD SSLARRHIAR E.QHPEYYKD C.
AGHU GA VI
            EREVLMWKFD SSLAREHVAR K.LYPEFFKD C.
AGU CD Z32
            EREVLMWKFD SSLARKHLAR E.MHPEFYKD ...
AJ_BW_BW21
            DREVLMWKFD SSLARRHLAR E.KHPEFYKD C.
  B AU VH
            EKEVLMWKFD SRLAVHHMAR E.LHPEYYKN ...
B CN RL42
            EREVLMWKFD SRLAIHHMAR E.MHPEYHKD C.
 B_DE_D31
            EREVLVWRFD SRLAFKHMAR E.LHPEYYKN ...
 B_DE_HAN
            EREVLKWKFD SHLAFHHKAR E.LHPEYYKD C.
B_FR_HXB2
            EREVLEWRFD SRLAFHHVAR E.LHPEYFKN C.
 B_GA_OYI
            EKEVLVWKFD SRLAFRHMAR E.VHPEYYKD C.
            EKEVLMWKFD SRLAFHHMAR E.KHPEFYKD C.
B_GB_CAM1
            EKEVLVWKFN SRLAFHHMAR E.LHPEFYKD C.
 B GB GB8
B GB MANC
            EKEVLVWKFD SRLAFHHVPD E.LHPEYYKD C.
  B KR WK
            EGEVLVWRFD SRLAFHHMAR E.KHPEYYKD C.
B NL 3202A
            EREVLEWRFD SRLAFHHMAR E.LHPEYYKD C.
B TW TWCYS
            EKEVLVWRFD STLAFHHRAR E.LHPEYYKX C.
   B US BC
            EREVLEWRFD SRLAFHHMAR E.LHPEYYKN R.
            EKEVLLWKFD SRLAYHHMAR E.LHPEYYKN C.
B US DH123
            EKEVLVWKFD SKLALHHVAR E.LHPEYYKD C.
B US JRCSF
B US MNCG
            EREVLVWKSD SHLAFQHYAR E.LHPEYYKN C.
B US P896
            EROVLVWRFD SRLAFHHVAR E.LHPEYFKN
   B US RF
            EKEVLVWKFD SRLAFHHVAR E.KHPEYYKD C.
 B_US_SF2
            EKEVLVWRFD SKLAFHHMAR E.LHPEYYKD C.
B US WEAU1
            EKEVLMWKFD SKLAFHHVAR E.LHPEYFKD C.
            EKEVLVWKFD SRLAFHHKAR E.LHPEYYKN
B US WR27
 B US YU2
            EREGLEWRFD SRLAFHHVAR E.LHPEYYKN
BF1 BR 93B
            DREILQWRFD SRLAFHHMAR E.LHPEYYKD C.
C_BR_92BR0
            HREVLOWKFD SLLARRHMAR E.LHPEYYKD C.
 BW 96BW0
            DGEVLRWKFD SHLAHRHMAR E.LHPEYYKD C.
 BW 96BW1
            HKEVLKWKFD SQLARRHLAR E.LHPEFYKD C.
            DREVLKWKFD SSLARRHLTR E.KHPEYYKD C.
 BW 96BW1
 BW_96BW1
            DKEVLMWKFD SHLARRHMAR E.LHPEYYKD C.
            DREVLKWKFD SHLARRHMAR E.LHPEYYKD C.
 ET ETH22
            HREVLKWKFD SQLARRHMAR E.LHPEFYKD C.
 _IN_93IN1
 _IN_93IN9
            HREVLOWKFD SLLAHRHRAR E.LHPEFYKD C.
C_IN_93IN9
            HREVLOWKFD SHLAHRHMAR E.LHPEYYKD C.
C_IN_94IN1
            HREVLMWK...QLAHRHIAR E.LHPEFYKD C.
C_IN_95IN2
            HNEVLVWKFD SQLAHKHRAR E.LHPEFYNK DC
            EREVLMWKFD SSLARRHIAR E.LRPEYYKD C.
CRF01_AE_C
CRF01_AE_C
            EREVLMWKFD SSLARRHIAR E.LHPEYYKD ...
            EREVLMWKFD SSLARRHIAR E.LHPEYYKD C.
CRF01_AE_C
            EREVLMWKFD SALARKHTAR E.LHPEYYKD C.
CRF01 AE T
CRF01 AE T
            EREVLMWKFD STLARKHIAR E.QHPEFYKD C.
            EREVLIWKFD SALARRHIAR E.LRPEFYKD C.
CRF01_AE_T
            EREVLMWKFD SALARKHIAR E.MHPEYYKD C.
CRF01_AE_T
            EREVLMWKFD SALARKHVAR E.QHPEYYKD C.
CRF01_AE_T
            EREVLIWKFD SSLARKHLAR E.LHPEYYKD C.
CRF01_AE_T
            DREVLVWRFD SSLARTHRAR E.LHPEYYKD C.
CRF02_AG_F
            DREVLVWRFD SSLARRHIAR E.RHPEFYKD C.
CRF02_AG_F
```

```
DREVLVWRFD SSLAFTHRAR E.MHPEFYKD C.
CRF02 AG G
CRF02 AG N DREVLIWRFD SRLAFRHTAR E.LHPEYYKD C.
CRF02 AG S DREVLVWRFD SRLAFTHKAR E.MHPEFYKD CX
CRF02 AG S DKEVLVWRFD SRLAFRHTAR E.LHPEYYKD C.
CRF03 AB R EKEVLMWKFD SRLALTHRAR E.LHPEFYKD C.
CRF03 AB R EKEVLMWKFD SRLALTHRAR E.LHPEFYKD C.
            EREVLKWKFD SRLAYKHVAR E.LHPEFYKD C.
CRF04_cpx_
CRF04_cpx_
            EREVLKWKFD SRLAFKHIAR E.LHPEFYKD C.
            EREVLKWKFD SLLAYRHMAR E.LHPEFYKD C.
CRF04_cpx_
CRF05 DF B DREVLQWKFD SSLALRHIAR E.RHPEFYQD ...
CRF05 DF B DGEVLRWKFD SSLALKHIAR E.RRPEFYQD ..
            EREVLKWKFD SSLARRHIAR E.KHPEFYKD C.
CRF06_cpx_
CRF06_cpx_
CRF06_cpx_
            EGEVLMWKFD SSLARRHIAR E.LHPDFYKD C.
            EREVLMWKFD SSLARRHTAR E.MHPEFYKD C.
CRF06_cpx_
            EXEVLMWKFD SSLARRHIAX E.XHPEFXKD C.
CRF11_cpx_ EREVLKWVFD SSLARKHIAR E.LHPDFYKD ..
CRF11_cpx_
D_CD_84ZR0
            DREVLRWKFD SSLARRHIAR E.LHPDFYKD ...
           EKEVLVWRFN SRLAFEHKAK E.KYPEYFKN C.
  D_CD_ELI
            ERQVLKWRFN SRLAFEHKAR E.MHPEFYKN ...
  D_CD_NDK ERQVLMWRFN SRLALEHKAR E.LHPEFYKD C.
D UG 94UG1 EREVLVWRFN SRLAFEHKAK M.KHPEYYKD C.
F1_BE_V185 DREVLRWKFD SSLALRHIAR E.RHPEFYQD ..
F1_BR_93BR DKEVLKWEFD SRLALRHIAR E.RHPEYYQD ..
F1 FI FIN9 DREVLKWKFD SRLALKHIAR E.RHPEFYRD ..
F1 FR MP41
            DREVLRWEFD SRLAFRHIAR E.KHPEFYQN ...
F2 CM MP25 DKEVLKWQFD SRLALRHIAR E.RHPEYYKD ..
F2KU BE VI EREVLVWKFD SRLALKHLAR E.KHPEYYKD C.
G BE DRCBL DGEVLVWRFD SSLARRHLAR E.LHPEYYKD C.
G NG 92NG0 DREVLVWRFN SSLARRHLAR E.LHPEYYKD C.
            DREVLVWRFD SSLARRHIAR E.LHPEYYKD C.
G SE SE616
H BE VI991
            EREVLMWKFD SRLALRHRAK E.LHPEFYKD C.
H BE VI997
            EGEVLMWKFD SRLAFTHTAR E.KHPEFYKD C.
H CF 90CF0
            GREVLMWKFD SRLALTHLAR V.KHPEY.KD C.
J SE SE702
            EREVLKWKFD SSLARRHIAR E.LHPEFYKD C.
J SE SE788
            EREVLOWKFD SSLARRHIAR E.LHPEFYKD C.
K CD EQTB1
            HREVLKWKFD SSLARKHVAR E.MHPEYYKD ...
            HREILMWKFD SSLARRHVAR E.LHPDYYKD ...
K_CM_MP535
            HKEVLVWRFD SSLARRHVAR E.LHPEFYKN C.
N_CM_YBF30
            HKEILMWKFD RSLGNTHVAM ITHPELFQKD ..
O_CM_ANT70
O CM MVP51
            HGEILKWQFD RSLGLTHIAL QKHPELFPSN ..
            HGQILKWQFD RSLGSTHVAM VTNPELFNKD
O SN MP129
            HKEMLKWQFD RSLGSTHVAL ITHPELFLKD ..
O SN MP130
U_CD 83C
            EKEVLMWKFD SSLARRHLAR E.LHPEFYKD C.
```

Table 14. HIV Pol Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

Name:	00BW0762_1		Len:	1046	Check:		Weight:	1.00
Name:	00BW0768_2	SEQ ID NO: 804	Len:	1046	Check:	8430	Weight:	1.00
Name:	00BW0874_2	SEQ ID NO: 805	Len:	1046	Check:		Weight:	1.00
Name:	00BW1471_2	SEQ ID NO: 806	Len:	1046	Check:	1324	Weight:	1.00
Name:	00BW1616_2	SEQ ID NO: 807	Len:	1046	Check:	935	Weight:	1.00
Name:	00BW1686_8	SEQ ID NO: 808	Len:	1046	Check:	8131	Weight:	1.00
Name:	00BW1759_3	SEQ ID NO: 809	Len:	1046	Check:	579	Weight:	1.00
Name:	00BW1773_2	SEQ ID NO: 810	Len:	1046	ChecK:	1975	Weight:	1.00
Name:	00BW1783_5	SEQ ID NO: 811	Len:	1046	Check:	216	Weight:	1.00
Name:	00BW1795_6	SEQ ID NO: 812	Len:	1046	Check:	5932	Weight:	1.00
Name:	00BW1811_3	SEQ ID NO: 813	Len:	1046	Check:	6525	Weight:	1.00
Name:	00BW1859_5	SEQ ID NO: 814	Len:	1046	Check:	2879	Weight:	1.00
Name:	00BW1880_2	SEQ ID NO: 815	Len:	1046	Check:	7093	Weight:	1.00
Name:	00BW1921_1	SEQ ID NO: 816	Len:	1046	Check:	2524	Weight:	1.00
Name:	00BW2036_1	SEQ ID NO: 817	Len:	1046	Check:	8279	Weight:	1.00
Name:	00BW2063_6	SEQ ID NO: 818	Len:	1046	Check:	3935	Weight:	1.00
Name:	00BW2087_2	SEQ ID NO: 819	Len:	1046	Check:	7898	Weight:	1.00
Name:	00BW2127_2	SEQ ID NO: 820	Len:	1046	Check:	728	Weight:	1.00
Name:	00BW2128_3	SEQ ID NO: 821	Len:	1046	Check:	5356	Weight:	1.00
Name:	00BW2276_7	SEQ ID NO: 822	Len:	1046	Check:	9456	Weight:	1.00
Name:	00BW3819_3	SEQ ID NO: 823	Len:	1046	Check:	6369	Weight:	1.00
Name:	00BW3842_8	SEQ ID NO: 824	Len:	1046	Check:	4573	Weight:	1.00
Name:	00BW3871_3	SEQ ID NO: 825		1046	Check:		Weight:	1.00
Name:	00BW3876_9	SEQ ID NO: 826	Len:	1046	Check:	6609	Weight:	1.00
Name:	00BW3886_8	SEQ ID NO: 827		1046	Check:	8244	Weight:	1.00
Name:	00BW3891_6	SEQ ID NO: 828	Len:	1046	Check:	5718	Weight:	1.00
Name:	00BW3970_2	SEQ ID NO: 829		1046	Check:	3940	Weight:	1.00
Name:	00BW5031_1	SEQ ID NO: 830		1046	Check:		Weight:	1.00
Name:	96BW01B21	SEQ ID NO: 831		1046	Check:	2358	Weight:	1.00
Name:	96BW0407	SEQ ID NO: 832	Len:	1046	Check:		Weight:	1.00
Name:	96BW0502	SEQ ID NO: 833	Len:	1046	Check:	3948	Weight:	1.00
Name:	96BW06_J4	SEQ ID NO: 834		1046	Check:	7173	Weight:	1.00
Name:	96BW11_06	SEQ ID NO: 835	Len:	1046	Check:	973	Weight:	1.00
Name:	96BW1210	SEQ ID NO: 836		1046	Check:	5817	Weight:	1.00
Name:	96BW15B03	SEQ ID NO: 837	Len:	1046	Check:	5157	Weight:	1.00
Name:	96BW16_26	SEQ ID NO: 838		1046	Check:	3303	Weight:	1.00
Name:	96BW17A09	SEQ ID NO: 839		1046	Check:		Weight:	1.00
Name:	96BWMO1_5	SEQ ID NO: 840		1046	Check:	5593	Weight:	1.00
Name:	96BWMO3_2	SEQ ID NO: 841		1046	Check:	3661	Weight:	1.00
Name:	98BWMC12_2	SEQ ID NO: 842		1046	Check:	7159	Weight:	1.00
Name:	98BWMC13_4	SEQ ID NO: 843		1046	Check:	3254	Weight:	1.00
Name:	98BWMC14_a		Len:		Check:		Weight:	1.00
Name:	_		Len:	1046	Check:		Weight:	1.00
Name:	_		Len:	1046	Check:		Weight:	1.00
	98BWM036_a		Len:	1046	Check:		Weight:	1.00
	98BWM037_d		Len:	1046	Check:		Weight:	1.00
Name:			Len:	1046	Check:		Weight:	1.00
Name:			Len:	1046	Check:		Weight:	1.00
Name:	_		Len:	1046	Check:		Weight:	1.00
Name:			Len:	1046	Check:		Weight:	1.00
Name:			Len:	1046	Check:		Weight:	1.00
	A2_CD_97CD		•	1046	Check:		Weight:	1.00
	A2_CY_94CY		Len:	1046	Check:		Weight:	1.00
Name:			Len:	1046	Check:		Weight:	1.00
	A2G_CD_97C			1046	Check:		Weight:	1.00
Name:	A_BY_97BL0	SEQ ID NO: 858	Len:	1046	Check:	2/24	Weight:	1.00

```
Check: 1835
Name: A_KE_Q23_A SEQ ID NO: 859 Len: 1046
                                                          Weight:
                                                                     1.00
Name: A_SE_SE659 <u>SEQ ID NO: 860</u> Len: 1046
                                                           Weight:
                                                                     1.00
                                             Check: 647
                                             Check: 263
                                                                     1.00
Name: A SE SE725 SEQ ID NO: 861 Len: 1046
                                                           Weight:
                                             Check: 2271
                                                           Weight:
                                                                     1.00
Name: A SE SE753 SEQ ID NO: 862 Len: 1046
                                                          Weight:
                                                                     1.00
Name: A SE SE853 SEQ ID NO: 863 Len: 1046
                                             Check: 5036
Name: A SE SE889 SEQ ID NO: 864 Len: 1046
                                             Check: 8414
                                                           Weight:
                                                                     1.00
                                             Check: 3268
                                                          Weight:
                                                                     1.00
Name: A SE UGSE8 SEQ ID NO: 865 Len: 1046
Name: A UG 92UG0 SEQ ID NO: 866 Len: 1046
                                                 Check: 2007 Weight:
                                                                          1.00
Name: A UG U455 SEQ ID NO: 867 Len: 1046
                                             Check: 2277
                                                           Weight:
                                                                     1.00
Name: AC IN 2130 SEQ ID NO: 868 Len: 1046
                                             Check: 5353
                                                           Weight:
                                                                     1.00
                                                           Weight:
Name: AC RW 92RW SEQ ID NO: 869 Len: 1046
                                             Check: 4695
                                                           Weight:
Name: AC SE SE94 SEQ ID NO: 870 Len: 1046
                                             Check: 4206
Name: ACD SE SE8 SEQ ID NO: 871 Len: 1046
                                             Check: 7281
                                                           Weight:
                                                                     1.00
Name: ACG BE VI1 SEQ ID NO: 872 Len: 1046
                                             Check: 1400
                                                           Weight:
                                                                     1.00
Name: AD SE SE69 SEQ ID NO: 873 Len: 1046
                                             Check: 4640
                                                           Weight:
                                                                     1.00
Name: AD SE SE71 SEQ ID NO: 874 Len: 1046
                                             Check: 1057
                                                           Weight:
                                                                     1.00
Name: ADHK_NO_97 SEQ ID NO: 875 Len: 1046
                                             Check: 3502
                                                                     1.00
                                                           Weight:
Name: ADK CD MAL SEQ ID NO: 876 Len: 1046
                                             Check: 2578
                                                           Weight:
                                                                     1.00
Name: AG BE VI11 SEQ ID NO: 877 Len: 1046
                                             Check: 8416
                                                           Weight:
                                                                     1.00
Name: AG_NG_92NG SEQ ID NO: 878 Len: 1046
                                             Check: 9397
                                                           Weight:
                                                                     1.00
Name: AGHU_GA_VI SEQ ID NO: 879 Len: 1046
                                             Check: 9562
                                                           Weight:
                                                                     1.00
Name: AGU_CD_Z32 SEQ ID NO: 880 Len: 1046
                                             Check: 8398
                                                           Weight:
                                                                     1.00
                                             Check: 3451
                                                           Weight:
                                                                     1.00
Name: AJ_BW_BW21 <u>SEQ ID NO: 881</u> Len: 1046
Name: B_AU_VH_AF SEQ ID NO: 882 Len: 1046
                                             Check: 2033
                                                           Weight:
                                                                     1.00
Name: B_CN_RL42_ <u>SEQ ID NO: 883</u> Len: 1046
Name: B_DE_D31_U <u>SEQ ID NO: 884</u> Len: 1046
                                                           Weight:
                                             Check: 1369
                                                                     1.00
                                             Check: 4607
                                                           Weight:
                                                                     1.00
Name: B_DE_HAN_U SEQ ID NO: 885 Len: 1046
                                             Check: 1771
                                                           Weight:
                                                                     1.00
Name: B_FR_HXB2_ <u>SEQ ID NO: 886</u> Len: 1046
                                             Check: 4569
                                                           Weight:
                                                                     1.00
Name: B_GA_OYI__ SEQ ID NO: 887 Len: 1046
                                            Check: 3682
                                                           Weight:
                                                                     1.00
Name: B_GB_CAM1_ SEQ ID NO: 888 Len: 1046
                                            Check: 3161
                                                           Weight:
                                                                     1.00
Name: B GB GB8 A SEQ ID NO: 889 Len: 1046
                                            Check: 6253
                                                           Weight:
                                                                     1.00
                                                                     1.00
                                                           Weight:
Name: B_GB_MANC_ <u>SEQ ID NO: 890</u> Len: 1046
                                            Check: 7670
Name: B KR WK AF SEQ ID NO: 891 Len: 1046
                                             Check: 8737
                                                           Weight:
                                                                      1.00
                                             Check: 2083
                                                           Weight:
                                                                      1.00
Name: B_NL_3202A SEQ_ID_NO: 892 Len: 1046
                                                                      1.00
                                             Check: 3056
Name: B TW TWCYS SEQ ID NO: 893 Len: 1046
                                                           Weight:
Name: B US BC LO SEQ ID NO: 894 Len: 1046
                                            Check: 3160
                                                           Weight:
                                                                      1.00
Name: B US DH123 SEQ ID NO: 895 Len: 1046
                                             Check: 1102
                                                           Weight:
                                                                      1.00
Name: B_US_JRCSF SEQ ID NO: 896 Len: 1046
                                             Check: 5571
                                                           Weight:
                                                                      1.00
                                             Check: 3988
                                                           Weight:
                                                                      1.00
Name: B_US_MNCG_ SEQ ID NO: 897 Len: 1046
                                             Check: 2465
Name: B_US_P896_ SEQ ID NO:
                             898 Len: 1046
                                                           Weight:
                                                                      1.00
Name: B US RF M1 SEQ ID NO: 899 Len: 1046
                                                           Weight:
                                                                      1.00
                                             Check:
Name: B US SF2 K SEQ ID
                         NO:
                             9<u>00</u> Len: 1046
                                             Check: 1754
                                                           Weight:
Name: B US WEAU1 SEQ ID NO:
                             901 Len: 1046
                                             Check: 2993
                                                           Weight:
                                                                      1.00
                             902 Len: 1046
                                             Check: 4098
                                                           Weight:
                                                                      1.00
Name: B_US_WR27_ SEQ ID NO:
Name: B US YU2 M SEQ ID NO: 903 Len: 1046
                                             Check: 5564
                                                           Weight:
                                                                      1.00
                                             Check: 4182
                                                                     1.00
Name: BF1 BR 93B SEQ ID NO: 904 Len: 1046
                                                           Weight:
Name: C BR 92BR0 SEQ ID NO: 905 Len: 1046
                                             Check: 5481
                                                                     1.00
                                                           Weight:
Name: C BW 96BW0 SEQ ID NO: 906 Len: 1046
                                             Check: 6833
                                                           Weight:
                                                                      1.00
Name: C_BW_96BW1 SEQ ID NO: 907 Len: 1046
                                             Check: 2166
                                                           Weight:
                                                                      1.00
Name: C_BW_96BW1 SEQ_ID_NO: 908 Len: 1046
Name: C_BW_96BW1 SEQ_ID_NO: 909 Len: 1046
                                             Check: 5817
                                                           Weight:
                                                                      1.00
                                                           Weight:
                                             Check: 5157
                                                                      1.00
Check: 3509
                                                           Weight:
                                                                      1.00
                                             Check: 5471
                                                           Weight:
                                                                      1.00
                                             Check: 4102
                                                           Weight:
                                                                      1.00
Name: C_IN_93IN9 SEQ ID NO: 912 Len: 1046
                                             Check: 3150
Name: C_IN_93IN9 SEQ ID NO: 913 Len: 1046
                                                           Weight:
                                                                      1.00
Name: C_IN_94IN1 <u>SEQ ID NO: 914</u> Len: 1046
                                             Check: 5157
                                                           Weight:
                                                                      1.00
                                             Check: 4641
                                                           Weight:
                                                                      1.00
Name: C_IN_95IN2 SEQ ID NO: 915 Len: 1046
Name: CRF01_AE_C SEQ ID NO: 916 Len: 1046
                                             Check: 87
                                                           Weight:
                                                                      1.00
Name: CRF01_AE_C SEQ ID NO: 917 Len: 1046
                                             Check: 3758
                                                           Weight:
                                                                      1.00
Name: CRF01_AE_C SEQ ID NO: 918 Len: 1046
                                             Check: 2775
                                                           Weight:
                                                                      1.00
```

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Weight:
                                                                     1.00
Name: CRF01 AE T SEQ ID NO: 919 Len: 1046
                                             Check: 1864
Name: CRF01 AE T SEQ ID NO:
                             920 Len: 1046
                                             Check: 7414
                                                          Weight:
                                                                     1.00
                                                                     1.00
Name: CRF01 AE T SEQ ID
                         NO:
                             921 Len: 1046
                                             Check: 7837
                                                          Weight:
Name: CRF01 AE T SEQ ID
                                                                     1.00
                         NO:
                             922 Len: 1046
                                             Check: 3529
                                                          Weight:
Name: CRF01 AE T SEQ ID
                                             Check: 7503
                                                          Weight:
                                                                     1.00
                         NO:
                             923 Len: 1046
                                             Check: 5730
                                                          Weight:
                                                                     1.00
Name: CRF01_AE_T SEQ ID
                             924 Len: 1046
                         NO:
                                                          Weight:
                                                                     1.00
Name: CRF02_AG_F SEQ
                             925 Len: 1046
                                             Check: 9432
                      ID
                         NO:
                                                          Weight:
                                                                     1.00
Name: CRF02 AG F SEQ
                                             Check: 2064
                      ID
                             926 Len: 1046
                         NO:
Name: CRF02 AG G SEQ
                                             Check: 9849
                                                          Weight:
                                                                     1.00
                             927 Len: 1046
                      ID
                         NO:
Name: CRF02 AG N SEQ
                                             Check: 1793
                                                          Weight:
                                                                     1.00
                      ID
                             928 Len: 1046
                         NO:
                                             Check: 4817
Name: CRF02 AG S SEQ ID NO:
                                                          Weight:
                                                                     1.00
                             929 Len: 1046
                                             Check: 1764
Name: CRF02 AG S SEQ
                                                          Weight:
                                                                     1.00
                      ID NO: 930 Len: 1046
                                             Check: 1695
                                                          Weight:
                                                                     1.00
Name: CRF03 AB R SEQ
                      ID NO:
                             931 Len: 1046
                                             Check: 1425
                                                                     1.00
Name: CRF03 AB R SEQ ID NO:
                             932 Len: 1046
                                                          Weight:
                                             Check: 8496
                                                          Weight:
                                                                     1.00
Name: CRF04_cpx_ SEQ ID NO:
                             933 Len: 1046
                                             Check: 2074
Name: CRF04_cpx_ SEQ
                      ID NO:
                             934 Len: 1046
                                                          Weight:
                                                                     1.00
                                             Check: 9245
                                                          Weight:
                                                                     1.00
Name: CRF04_cpx_ SEQ ID NO: 935 Len: 1046
Name: CRF05 DF_B SEQ ID NO: 936 Len: 1046
                                             Check: 62
                                                          Weight:
                                                                     1.00
                                             Check: 3427
                                                          Weight:
                                                                     1.00
Name: CRF05_DF_B SEQ ID NO: 937 Len: 1046
Name: CRF06_cpx_ SEQ ID NO: 938 Len: 1046
                                                          Weight:
                                             Check: 142
                                                                     1.00
Name: CRF06_cpx_ SEQ ID NO: 939 Len: 1046
                                                          Weight:
                                             Check: 6688
                                                                     1.00
                                             Check: 8524
                                                          Weight:
                                                                     1.00
Name: CRF06_cpx_ <u>SEQ ID</u>
                         NO: 940 Len: 1046
Name: CRF06_cpx_ SEQ ID
                         NO: 941 Len: 1046
                                             Check: 4725
                                                          Weight:
                                                                     1.00
                                             Check: 2194
                                                          Weight:
                                                                     1.00
Name: CRF11_cpx_ <u>SEQ ID</u>
                         NO: 942 Len: 1046
Name: CRF11_cpx_ <u>SEQ ID</u>
                         NO: 943 Len: 1046
                                             Check: 8466
                                                          Weight:
                                                                     1.00
                                                                     1.00
Name: D_CD_84ZR0 SEQ ID
                         NO: 944 Len: 1046
                                             Check: 515
                                                          Weight:
                                             Check: 2096
                                                                     1.00
                                                          Weight:
Name: D CD ELI K SEQ ID
                         NO: 945 Len: 1046
                                                          Weight:
                                                                     1.00
                                             Check: 3376
Name: D CD NDK M SEQ ID
                         NO:
                             946 Len: 1046
                                             Check: 3505
                                                          Weight:
                                                                     1.00
Name: D UG 94UG1 SEQ ID
                         NO:
                             947 Len: 1046
                                                                     1.00
Name: F1 BE VI85 SEQ ID
                             948 Len: 1046
                                             Check: 3993
                                                          Weight:
                         NO:
                                                                     1.00
Name: F1 BR 93BR SEO ID
                             949 Len: 1046
                                             Check: 2251
                                                          Weight:
                         NO:
Name: F1 FI FIN9 SEQ ID
                             950 Len: 1046
                                             Check: 9772
                                                          Weight:
                                                                     1.00
                         NO:
Name: F1 FR MP41 SEQ ID
                         NO:
                             951 Len: 1046
                                             Check: 1447
                                                          Weight:
                                                                     1.00
                                             Check: 2842
                                                          Weight:
                                                                     1.00
Name: F2 CM MP25 SEQ ID
                         NO:
                             952 Len: 1046
                                             Check: 5026
                                                          Weight:
                                                                     1.00
Name: F2KU BE VI SEQ ID
                         NO:
                             953 Len: 1046
                                                          Weight:
                                                                     1.00
Name: G BE DRCBL SEQ
                      ID
                         NO:
                             954 Len: 1046
                                             Check: 5377
                         NO:
Name: G NG 92NG0 SEQ
                      ID
                             955 Len: 1046
                                             Check: 6000
                                                          Weight:
                                                                     1.00
                      ID
                             956 Len: 1046
                                             Check: 7901
                                                          Weight:
                                                                     1.00
Name: G SE SE616 SEQ
                         NO:
Name: H BE VI991 SEQ
                      ID
                         NO:
                             957 Len: 1046
                                             Check: 9107
                                                          Weight:
                                                                     1.00
                                             Check: 5776
                                                          Weight:
                                                                     1.00
Name: H BE_VI997 SEQ
                      ID
                         NO:
                             958 Len: 1046
Name: H CF 90CF0 SEQ ID
                             959 Len: 1046
                                             Check: 9201
                                                          Weight:
                                                                     1.00
                         NO:
                                             Check: 9700
                                                          Weight:
                                                                     1.00
Name: J SE SE702 SEQ
                             960 Len: 1046
                      ID
                         NO:
Name: J SE SE788 SEQ
                             961 Len: 1046
                                             Check: 8817
                                                          Weight:
                                                                     1.00
                      ID NO:
Name: K CD EQTB1 SEQ ID NO: 962 Len: 1046
                                             Check: 3723
                                                          Weight:
                                                                     1.00
Name: K CM MP535 SEQ ID NO:
                             963 Len: 1046
                                             Check: 3729
                                                          Weight:
                                                                     1.00
Name: N_CM_YBF30 SEQ ID NO:
                             964 Len: 1046
                                                                     1.00
                                             Check: 3336
                                                          Weight:
Name: O_CM_ANT70 SEQ_ID_NO:
                             965
                                 Len: 1046
                                             Check: 9461
                                                          Weight:
                                                                     1.00
Name: O_CM_MVP51 SEQ ID NO:
                             966 Len: 1046
                                             Check: 2986
                                                          Weight:
                                                                     1.00
Check: 377
                                                          Weight:
                                                                     1.00
                                             Check: 9312
                                                          Weight:
                                                                     1.00
                                             Check: 1358
                                                          Weight:
                                                                     1.00
//
                                                                           50
SEQ ID NO
                     MGGKWSKSS. IVGWPAVRER IR....RTDP ..........AAEGVG
         00BW0762_1
636
                     MGGKWSKSSI V.GWPEVRER IRR..TEP.. ............AAEGVG
         00BW0768 2
637
                     MGGKWSKSS. LTGWPAVRER IR....RTEP ...........AAEGVG
         00BW0874 2
638
         00BW1471 2
                     MGGKWSKSS. IVGWPAVKER IRR..TNPR. ..... .TERAAVGVG
639
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640	00BW1616_2			MRRAEP		
<u>641</u>	00BW1686_8	MGGKWSKRS.	KADWPAVREK	LRTTEP		AAEGVG
642	00BW1759_3	MGNKWSKS	WPAVRER	IRRTRPAR		GNEPAAEGVG
<u>643</u>	00BW1773_2	MGSKWSKSSI	V.GWPKVRET	IRRTEP		AAEGVG
644	00BW1783_5	MGNKWSKS	WPAIRER	IRRTNPAA		ERTRAAEGVG
645	00BW1795_6	MGGKWSKSS.	VVGWPAIRER	MRR		. TEPAAEGVG
646	00BW1811_3	MGGKWSKSC.	KIGWPAVRER	MRR		.TEPAVEGVG
647	00BW1859_5	MGGKWSKSG.	KVGWPEVRER	MRRTRPAA	EGG	DSAAEGVG
648	00BW1880_2	MGGKWSKSS.	LVGWPAVRER	IRTTAP		
649	00BW1921_1	MGGKWSKSS.	IVGWPAVRER	MRKTEP		AAEGVG
650	00BW2036_1	MGGKWSKSS.	IVGWPAVRER	IRR		. TEPAAEGVG
651	00BW2063_6	MGGKWSKSSI	I.GWPAVRER	MRKAEP		AAEGVG
 652	00BW2087_2	MGSKWSKSS.	IVGWPAVRER	IRRT		RTEPAAEGVG
 653	00BW2127 2	MGGKWSKSSI	I.GWPAIRER	IRRTEP		AAEGVG
 654	00BW2128 3	MGSKWSKCSI	I.GWPAVRER	IRRAEP		AAVGVG
 655	 00BW2276 7	MGSKWSKC	.SGWPDVRER	MRRATPAA	EAGRAAP	AAEGAAPGVG
 656	00BW3819 3	MGSKWSKCSI	V.GWPDVRER	MRRARPAV	RERRRQTEPA	AEGVAAEGVG
657	00BW3842 8	MGGKWSKGR.	IVGWPAVRER	MRR		. TEPAAEGVG
 658	00BW3871 3	MGSKWSKRS.	IVEWPAVRER	LRKTEP		AAEGVG
659	00BW3876 9					AAEGV G
660	00BW3886 8			MKRTEP		
661	00BW3891 6			MRRTQP		
662	00BW3970 2			MRRTQPAA		
663	00BW5031 1			IRRTDP		
664	96BW01B21			IRRTEP		
665	96BW0407			MRRAEP		
666	96BW0502	MGGKWSK	CSGWPAVRER	MRRTRPAV	EGR	. TESAAEGVG
667	96BW06 J4			IRRTDP		
668	96BW11 06			IRRTEPAA		
669	96BW1210			IRRTEPAT		
670	96BW15B03			IRR		
671	96BW16 26			MRRTR		
672	96BW17A09			IRRTNPLT		
673	96BWMO1 5			IRKTEPRK		
674	96BWMO3 2	MGGKWSKSS.		MRRTRPGA		
675	98BWMC12 2			MRRTEP		
575 676	98BWMC13 4			MRR		
677	98BWMC14 a			IRKPRP		
678	98BWM014 1			LR		
679	98BWM018 d			IRQTDPRE		
680	98BWM036 a			IRRTEPRR		
	_	MGGKWSKSS:		LRRTAP		
681 682	98BWMO37_d			LRRTEP		
682 683	99BW3932_1			IRRTQPAA		
<u>683</u>	99BW4642_4			IRQAEP		
684	99BW4745_8			MRR		
685	99BW4754_7			IRRTEPAV		
<u>686</u>	99BWMC16_8	MGNKWSKS	WPAVKER	IKKIEPAV	rvR	KIEPAAEGVG

687	A2_CD_97CD	мсскискот	TVCWDETDED	мрр трраа	EGVR	PTPPAAEGVG
688	A2_CY 94CY				TE	
	A2_C1_94C1 A2D 97KR				TP	
<u>689</u>						
<u>690</u>	A2G_CD_97C					
<u>691</u>	A_BY_97BL0					
692	A_KE_Q23	MGGKWSKSS.				
<u>693</u>	A_SE_SE659					
694	A_SE_SE725					
<u>695</u>	A_SE_SE753					
<u>696</u>	A_SE_SE853					
<u>697</u>	A_SE_SE889					
<u>698</u>	A_SE_UGSE8					
<u>699</u>	A_UG_92UG0				RTR	
700	A_UG_U455				• • • • • • • • • •	
· <u>701</u>	AC_IN_2130					
702	AC_RW_92RW					
703	AC_SE_SE94	$\mathtt{MGGKWSKSS}$.	IIGWPQIRER	IRRTPP		AATGVG
704	ACD_SE_SE8	MGGKWLKSSI	V.GWPAVRER	IRRTEP		AAEGVG
<u>705</u>	ACG_BE_VI1	MGGKWSKRS.	KVEWPQVRER	MRQTPIAA	$\mathtt{EA}.\dots.\mathtt{EG}$	AAAEGVG
706	AD_SE_SE69	MGGKWSKSS.	IVGWPAVRER	IKRT		DPAAEGVG
707	AD_SE_SE71	MGGKWSKSS.	IVGWPEVRER	MRRARAP		SAAPGVG
708	ADHK_NO_97	MGGKWSKSS.	IVGWPAIRER	MRRAEP		AAEGVG
709	ADK CD MAL	MGGKWSKSS.	IVGWPKIRER	IRRTPPTETG		VGAVSQD
710	AG BE VI11	MGGKWSKSS.	PVGWSRVRER	MRRTPPAA	EG	AAAEGVG
711	AG NG 92NG	IGGKWSKSS.	IVGWPAVRER	IRQTP		PAEGVG
712	AGHU GA_VI	MGGEWSRSS.	IVGWSTIRER	MRRAEP		AAAGVG
713	AGU_CD_Z32	MGNKWSKG	WPAVRER	IRQTPPAP	P	AAEGVG
714	AJ BW BW21	MGSNWSKS.S	IIGWPQVRER	MKRAP	A	AAEGVG
715	B AU VH	MGGKGSKRI.	RSEWPTVRER	IIQAEPAA	AG	VG
716	B_CN_RL42				DG	
717	— — В DE D31	MGGKWSKSS.	VVGWPAIRER	мк		RAEPAAEGVG
718	B_DE_HAN	MGGKWSK	CSGWPTVRER	MKQAEP		EPAADGVG
719	B FR HXB2			·-		
720	B GA OYI				PE	
721	B GB_CAM1					
722	B_GB_GB8					
	B_GB_MANC				EGRKK	
723	B KR_WK				EG	
724	B_NL_3202A					
<u>725</u>	B_NL_3202A B TW TWCYS					
<u>726</u>						
727	B_US_BC				DR	
728	B_US_DH123					
<u>729</u>	B_US_JRCSF				DRVR	
730	B_US_MNCG					
<u>731</u>	B_US_P896					
732	B_US_RF				DG	
<u>733</u>	B_US_SF2	MGGKWSKRS.	MGGWSAIKER	MKKAEP	• • • • • • • • • •	CAEPAADGVG

724	D HC WEALL	MCCTHCVDC	CCCWDATRER	MED VEDVV	EG	VC
<u>734</u>	B_US_WEAU1					
<u>735</u>	B_US_WR27					
<u>736</u>	B_US_YU2				ERMR	
<u>737</u>	BF1_BR_93B				• • • • • • • • •	
<u>738</u>	C_BR_92BR0					
<u>739</u>	C_BW_96BW0					
<u>740</u>	C_BW_96BW1				EGV	
<u>741</u>	C_BW_96BW1				• • • • • • • • • • •	
<u>742</u>	C_BW_96BW1					
743	C_ET_ETH22					
<u>744</u>	C_IN_93IN1	MGGKWSKCSI	V.GWPAIRER	MRRAEP		AAEGVG
<u>745</u>	C_IN_93IN9	MGGKWSKCSI	V.GWPDIRER	MRRTQP		AAEGVG
746	C_IN_93IN9	MGGKWSKCSI	V.GWPAVRER	MRRTEP		AAEGVG
747	C_IN_94IN1	MGGKWSKCSI	V.GWPEIRER	MRRTQP		AADGVG
748	C_IN_95IN2	MGGKWSKCSI	V.GWPDIRER	MRRTEP		AAEGVG
749	CRF01_AE_C	MGGKWSKN.R	IVGWPQVRER	IRRTPAAA		EGVG
 750	CRF01 AE C	MGGKWSKSC.	IVGWPQVRER	IRQTPVAE	ER	QTPAAAEGVG
751	CRF01 AE C	MGNKWSKS	WPQIRER	IRQTPVAT		EGVG
 752	CRF01 AE T					
 753	CRF01 AE T					
754	CRF01 AE T					
755	CRF01 AE T					
755 756	CRF01 AE T					
750 757	CRF01 AE T					
757 758	CRF01_AB_1					
750 759	CRF02 AG F					
7 <u>55</u> 760	CRF02 AG G					
761	CRF02_AG_U					
						
<u>762</u>	CRF02_AG_S					
<u>763</u>	CRF02_AG_S					
764	CRF03_AB_R					
<u>765</u>	CRF03_AB_R					
<u>766</u>	CRF04_cpx_				ERMRRA	
<u>767</u>	CRF04_cpx_					
768	CRF04_cpx_				A	
<u>769</u>	CRF05_DF_B				• • • • • • • • •	
<u>770</u>	CRF05_DF_B				-	
<u>771</u>	CRF06_cpx_				R	
<u>772</u>	CRF06_cpx_				G	
<u>773</u>	CRF06_cpx_				G	
<u>774</u>	CRF06_cpx_			-	ER	
<u>775</u>	CRF11_cpx_				T	
<u>776</u>	CRF11_cpx_	MGGNWSKS.S			T	
<u>777</u>	D_CD_84ZR0	MGGKWSKSS.			RR	
<u>778</u>	D_CD_ELI				• • • • • • • • • • • • • • • • • • • •	
<u>779</u>	D_CD_NDK				• • • • • • • • • • • • • • • • • • • •	
<u>780</u>	D_UG_94UG1	MGGKWSKSS.	IVGWPAVRER	MRRT	• • • • • • • • • • • • • • • • • • • •	EPAAEGVG

```
F1 BE VI85
781
                MGGKWSKSS. IVGWPAIRER MRR..TPPT. ...... ..PPAAEGVG
       F1 BR 93BR
782
                MGGKWSKSS. IVGWPAIRER MRR..PP... ...... ..PAAAEGVG
783
       F1 FI FIN9
                784
       F1 FR MP41
                MGGKWSKSS. IVGWPAIRER IRR..TP... ............VAAEGVG
785
       F2_CM_MP25
                MGGKWSK.....GWPSVRER IRR..TPPAA P.........AADGVG
       F2KU BE VI
786
787
                MGNKWSKRK. VAGWPEVRER LR...QHPA. ............AAEGVG
       G BE DRCBL
                MGGKWSKSS. IVGWPQIRER IR...QTPV. ...... AAEGVG
788
       G NG_92NG0
                MGGKWSKSS. IVGWPEVRER IR...NTPT. ...... AAEGVG
       G_SE_SE616
789
                MGGKWSKGC. ISGWPAVRER IRQ..TEP.......AAEGVG
       H_BE_VI991
790
                MGGKWSKSS. IVGWPAVRER IRR..AQP.. ..... AADGVG
791
       H BE VI997
                MGGKWSKSR. MGGWSTIRER MRR..AEP.. .....VAEGVG
       H CF 90CF0
792
                MGNKWSKS.....WPOVRDR MRR..A..AP A.....P ....AADGVG
793
       J SE SE702
                MGNKWSKS.....WPQVRER MRR.....AP A......P ....AADGVG
794
       J SE SE788
                MGGKWSKS.S IVGWSTVRER MR...... KTPPAADGVG
795
       K_CD_EQTB1
                MGGKWSKS.S IVGWPAIRER MRR..ARPAA DR.....V GTQPAADGVG
       K CM MP535
796
                MGKIWSKSS. LVGWPEIRER MRRQTQEP.. ..... .AVEPAVGAG
797
       N CM YBF30
                MGNALRKGK. FEGWAAVRER MRRTRTF.... P ESEPCAPGVG
       O CM ANT70
798
                MGNAWSKSK. FAGWSEVRDR MRRSSS.... D PQQPCAPGVG
       O CM MVP51
799
                MGNVLGKDI. FKGWSAVRER MRGTS..... P DPEPCAPGVG
800
       O SN MP129
                MGNVLGKDK. FKGWSAVRER MRKTS..... P EPEPCAPGVG
       O SN MP130
801
                MGNKWSKQ.....WPAIRER MRR..ARPAA E......P ....AADGVG
       U CD 83C
802
00BW0762 1
         LQVR..... GTLNFPQITL
         LQVRG..... GTLNCPQITL
00BW0768 2
         PQARAISPTS REPOVRRDN. ....SRFEAG VEREG..... .TLNFPQITL
00BW0874 2
         00BW1471 2
         LOVR..... GTLNFPQITL
00BW1616 2
         LOVR..... GTLNLPQITL
00BW1686 8
00BW1759_3
         LQVRG..... GNLNFPQITL
00BW1773_2
         LQVR..... GTLNFPQITL
         LQVR.....GDN....PCSEAG DERQ....GTFNFPQITL LQVR.....GDN....PLSEAG AERQ.....GTLNFPQITL
00BW1783_5
00BW1795_6
         LQVR........GDN. ....PRFEAG EKRQG......NLNFPQITL
00BW1811_3
00BW1859 5
         LQVR..... GTLNFPQITL
         LQVR..... GTLNFPQITL
00BW1880_2
         00BW1921_1
00BW2036_1
         LQVR..... GTLNFPQITL
         L..R..... GDN. ....PCSEAG DERQ..... GTLNFPQITP
00BW2063_6
         NSPTSREL.. ...QVRGDN. ....PSIKAG PERQ..... GALNFPQITL
00BW2087_2
         LQVR........GDN. ....PRSEAG AERQG..... .SLNFPQITL
00BW2127 2
         LQVR..... GTLNFPQITL
00BW2128 3
         LQVR........GDN.....PRAEAG AERQG......TLNFPQITL
00BW2276_7
         LQVR.......GDN. ....PRSEAG DERQG..... ALNFPQITL
00BW3819 3
         LQVR...... GDN. ....PRSEAG AERQGT..LQ GTLNFPQITL
00BW3842 8
         LQVR..... GTLNFPQITL
00BW3871 3
         LQVR..... GTLNFPQITL
00BW3876 9
         LQVR.......GDN. ....PRSEAG AERQG..... .SLNFPQITL
00BW3886 8
         LQVR.......GDN. ....PRSEAG AERQG..... .TLNFPQITL
00BW3891 6
         LQVR.......GDN. ....PRSETG AEGQG..... .TFNFPQITL
00BW3970 2
00BW5031 1
         LOVR..... ......GDN. ....PRSEAG DEREG.... .TLNFPQITL
         96BW01B21
         LQVR........GDN. ....PRSETR VEGQG......NFNFPQITL
 96BW0407
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			_			
96BW0502	LQVR				AEGQGTLQ	
96BW06_J4	LQIR		1	PRFEAG	TKRQ	GTLNFPQITL
96BW11 06	LRG	NN.	1	PCSEAG	DERQ	GTLNFPQITL
96BW1210	LOVR	GDN.		PCSEAG	AEGQG	TTFSFPQITL
96BW15B03	LQVR				AERO	GTLNFPOITL
96BW16 26	LQVW				AKGQ	GTFNFPQITL
_	LQVR				AERQG	.TLNFLQITL
96BW17A09		GDN.				
96BWMO1_5					DERQGTLQ	
96BWMO3_2		TNSP.			VEGQG	.TLNFPQITL
98BWMC12_2		QARGDN.			DEGQG	
98BWMC13_4	PR				AERQ	
98BWMC14_a	LQVR	GDN.			AEGQ	~
98BWM014 1	LQVREQTR	ANSSTS.	1	RELQAG	AKRQ	GALNCPQITL
98BWM018 d	LQVR	GDN.	1	PCSEAG	AERQGS	.TLNFPQITL
98BWMO36 a	LOVR	GDK.	1	PRSEAG	AEGQG	.TLNFPQITL
98BWM037 d	LQVR				GERQG	
99BW3932 1		GDN.			AERQG	
99BW4642_4		GDD.			AERQ	
		GDD.			AERQG	
99BW4745_8						
99BW4754_7		GDN.			VKGQ	
99BWMC16_8		GDK.			VEKQG	
A2_CD_97CD		DN.			EQGAV	
A2_CY_94CY		DN.			TGDQGTI	
A2D 97KR	LWNGGG	DN.	1	PLAEAG	AEKQGTT	HSCNFPQITL
A2G CD 97C	PRVRR		1	LLPEAG	DEGKGAV	YPCNFPQITL
A BY 97BL0	LD.GGR	DN.	1	PLPETG	TERQGTV	SSFNFPQITL
A KE Q23 A	LWDGGR				AERQGTG.	
A_SE_SE659		DS.			ADP	
A_SE_SE033 A SE SE725		DS.			AERQGT . E.	_
	LWNEGR				AEGTR.	PTFSFPQITL
A_SE_SE753		DN.			AERQGTG.	PTLSFPQITL
A_SE_SE853						
A_SE_SE889	LWDGGR				EERQGVGG	TTLNFPQITF
A_SE_UGSE8		DS.			AKQP	.TFSFPQITL
A_UG_92UG0		DS.			AERQGPE.	PTFSFPQITL
A_UG_U455_		DD.			AERQGT	
AC_IN_2130		\dots GDN.			AKRQG	
AC_RW_92RW		RDS.]	LSSETG	AERQG	.TFNFPQITL
AC SE SE94	LRDGGR	D		.NSEAG	TDRQGTG.	PAFSFPQITL
ACD SE SE8	LRVWRR	DN.	:	PLPEAG	AERQGT	VSFSLPQITL
ACG BE VI1		DR.		LLPEAG	TEGQGTI	SSFNFPQITL
AD SE SE69		DS			AERQGA	
	T.WDGGP	DS.				
AD_SE_SE71 ADHK NO 97		DN				
		DK				
ADK_CD_MAL						
AG_BE_VI11		DN.			TEGHGTI	
AG_NG_92NG		GDS.			AEGKGIT	
AGHU_GA_VI		GDS.			AKGKGA	
AGU_CD_Z32		GDN.			TEGQGTI	
AJ_BW_BW21	LRVWR	GDS.		PLPEAG	GEGQGT	VSFNFPQITL
B AU VH AF	LQVWGR	DNN.	:	SLSEAG	ADRQGT	VSFSFPQITL
B CN RL42	LQVWGR	\dots DNN.	:	SISEAG	ADRQGT	ISFSFPQITL
B DE D31 U	LQVWGR	DSN.	:	SLSEAG	ADRQGT	VSFSFPQITL
B DE HAN U	LOVWG	sns.		SLSEAG	ADRQGT	VSLSLPQITL
B_FR_HXB2_		DNN.			ADRQGT	
B GA OYI		DNN.			ADRQGT	
B GB CAM1		ENN.			ADRQGT	
B GB GB8 A		DNN.			ADKQGT	
		DNN.				
B_GB_MANC_						
B_KR_WK_AF		DNN.				
B_NL_3202A	пÕлмGК	DNN.	• • • • •	SUSEAG	AEGQGT	ASPSPAGLLP

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B US DH123
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B US JRCSF
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B US P896
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B US SF2 K
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C BR 92BR0
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 BW 96BW0
          LRG..... PCSEAG DERQ.....
                                                GTLNFPQITL
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K CD EOTB1
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K CM MP535
N CM YBF30
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O CM ANT70
           GSEGTR.... A VPICLPQIPL
O CM MVP51
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D CD ELI K
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           SAGERIVDII ATDLQTKELQ KQITKIQNFR VYYRDSRDPI WKGPAKLLWK
CRF11_cpx_
           SAGERIIDII ATDLQTKELQ KQITKIQKFR VYYRDSRDPI WKGPAKLLWK
CRF11 cpx
           SAGERIIDII ASDIQTRELQ KQITKIQNFR VYYRDSRDPI WKGPAKLLWK
D CD 84ZR0
           SAGERIIDII ATDIQTKELQ KQIIKIQNFR VYYRDSRDPI WKGPAKLLWK
D CD ELI K
           SAGERIIDII ATDIQTRELQ KQIIKIQNFR VYYRDSRDPI WKGPAKLLWK
D CD NDK M
           SAGERIIDII ATDIQTKELQ KQIIKIQNFR VYYRDSRDPV WKGPAKLLWK
D UG 94UG1
           SAGERIIDII STDIQTRELQ KQITKIQNFR VYYRDSRNPV WKGPAKLLWK
F1 BE VI85
           SAGERTIDII ATDIQTRELQ KQIIKIQNFR VYYRDSRDPV WKGPAKLLWK
F1_BR_93BR
           SAGERIIDII ATDIQTKELQ KQVTKIQNFR VYYRDSRDPV WKGPAKLLWK
F1 FI FIN9
           SAGERIIDII STDIQTRELQ KQIIKIQNFR VYYRDSRDPV WKGPAKLLWK
F1 FR MP41
F2_CM_MP25
           SAGERIIDII ATDIQTKELQ KQISKIQNFR VYFRDSRDPV WKGPAKLLWK
           SAGERIVDII ASDIQTRALQ KQITKIQNFR VYYRDSRDPI WKGPAKLLWK
F2KU_BE_VI
           SAGERIIDII ASDIQTKELQ KQITKIQNFR VYYRDSRDPI WKGPAKLLWK
G_BE_DRCBL
G_NG_92NG0 SAGERIIDII ASDIQTKELQ KQIIKIQNFR VYYRDSRDPI WKGPAKLLWK
G_SE_SE616 SAGERIIDII ASDIQTKELQ KQITKIQNFR VYYRDSRDPV WKGPAKLLWK
H_BE_V1991 SARERIIDII ATDIPTKELQ KQISQIQKFR VYYRDSRDPI WKGPAKLLWK
H_BE_V1997 SAGERIIDII ATDIQTKELQ KQISNIQKFR VYYRDSRDPI WKGPAKLLWK
H_CF_90CF0 SAGERIIDII ATDIQTKELQ KQISNIQKFR VYYRDSRDPI WKGPAKLLWK
J SE SE702 SAGERIIDII ATDIQTKELQ KQITKIQNFR VYYRDSRDPI WKGPAKLLWK
J SE SE788 SAGERIIDII ATDIQTRELQ KQITKIQNFR VYYRDSRDPI WKGPAKLPWK
K CD EQTB1 SAGERIIDII ATDIQTKELQ KQITKIQNFR VYYRDSREPI WKGPAKLLWK
            SAGERIVDII ATDIQTKELQ KQILNIQKFR VYYRDSREPI WKGPAKLLWK
K CM MP535
           TAGERIIDII ATDIQTTNLQ TQILKVQNFR VYYRDSRDPI WKGPAKLLWK
N CM YBF30
            TAGERIIDIL ASQIQTTELQ KQILKXHKFR VYYRDSRDPI WKGPAQLLWK
O CM ANT70
            TAGERLIDIL ASQIQTTELQ KQILKINNFR VYYRDSRDPI WKGPAQLLWK
O CM MVP51
            TAGERIIDIL ASQIQTTELQ KQIFKIQKFQ VYYRDSRDPI WKGPAQLLWK
O SN 99SE
            TAGERIIDIL ASQIQTTELQ KQIFKIQKFQ VYYRDSRDPI WKGPAQLLWK
O SN 99SE
U CD 83C SAGERIIDII ATDIQTKELQ KQITKIQNFR VYYRDSRDPI WKGPAKLLWK
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1046 1001 00BW0762 1 GE.GAVVIQD NSDIKVIPRR KAKIIKDYGK QMAGADCVAG RQDED. 00BW0768 2 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED. 00BW0874 2 GE.GAVVIQD NGDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED. 00BW1471 2 GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAG RQDED. 00BW1616 2 GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGADCVAG RQDED. 00BW1686 8 GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAG RQDEDQ 00BW1759 3 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDEDQ OOBW1773_2 GE.GAVVIQD NNDIKVVPRR KVKIIKGYGK QMAGADCVAG GQDEN.

OOBW1783_5 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCMAG RQDEDQ

OOBW1795_6 GE.GAVVIQD NSEIKVVPRR KVKIIRDYGK QMAGADCVAG RQDEDQ

OOBW1811_3 GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGADCVAG GQDEN.

OOBW1859_5 GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAS RQDED.

OOBW1880_2 GE.GAVVIQD KSDIKVVPRR KVKIIRDYGK QMAGADCVAD RQDED.

OOBW1921_1 GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAD RQDED.

OOBW2036_1 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED.

OOBW2063_6 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED.

OOBW2087_2 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED.

OOBW2127_2 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED.

OOBW2128_3 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG GQDEN.

OOBW2276 7 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG GQDEN. 00BW1773_2 GE.GAVVIQD NNDIKVVPRR KVKIIKGYGK QMAGADCVAG GQDEN. 00BW2276_7 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED. 00BW3819_3 GE.GAVVIQD NGDIKVVPRR KAKIIKDYGK QMAGADCVAS RQDEN. 00BW3842 8 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED. 00BW3871_3 GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED. 00BW3876 9 GE.GAVVIQD NSDIKVVPRR KAKIIKNYGK QMAGADCVAG RQDED. 00BW3886 8 GE.GAVVIQD KGDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED. 00BW3891 6 GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGDDCVAG RQDED. 00BW3970 2 GE.GAVVIQD NSDIKVVPRR RAKIIRDYGK QMAGADCVAD RQDED. 00BW5031 1 GE.GAVVIQD NSDIKAVPRR KAKIIKDYGQ QMAGADCVAG RQDEN. 96BW01B21 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED. 96BW0407 GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGDDCVAG RQDED. 96BW0502 GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG GQDEN. 96BW06_J4 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAS RQDED. 96BW11 06 GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGADCVAG RQDED. 96BW1210 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED. 96BW15B03 GEGAVVVIQD NSDIKVVPRR KVKIIRDYGK QMAGADCVAG RQDED. 96BW16_26 GE.GAVVLQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG GQDEN. 96BW17A09 GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAG RQDED. 96BWMO1_5 GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGADCVAG RQDEDQ 96BWMO3_2 GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAG RQDEDQ 98BWMC12_2 GD.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAG RQDED. 98BWMC13_4 GE.GAVVIQD NSEIKVVPRR KVKIIRDYGK QMAGADCVAG RQDEDQ 98BWMC14_a GE.GAVVIQD SSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED. 98BWMO14_1 GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED. 98BWMO18_d GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDEDQ 98BWMO36_a GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG GQDED. 98BWMO37_d GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAG RQDEDQ 99BW3932_1 GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAS RQDED. 99BW4642_4 GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAD RQDED. 99BW4745_8 GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED. 99BW4754_7 GE.GAVVIQD KSDIKVVPRR KAKIIKDYGK QMAGDDCVAG RQDED. 99BWMC16_8 GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED. A2 CD 97CD GE.GAVVIQD NGDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED. A2_CY_94CY GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED. A2D 97KR GE.GAVVIQD NSDIKVVPRR RAKIIRDYGK QMAGDDCVAG RQDED. A2G CD 97C GE.GAVVIQD NNEIKVVPRR KTKILRDYGK QMAGDDCVAG RQDED. A BY 97BLO GE.GAVVIQD NXDIKVVPRR KAKIIXDXXK QMAGXDCVAS RQDED. A_KE_Q23_A GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED. A SE_SE659 GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED. A_SE_SE725 GE.GAVVIQD NNDIKVVPRR KAKILRDYGK QMAGDDCVAG RQDED.

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GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGDDCVAG RQDED.
A SE SE753
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
A SE SE853
           GE.GAVLIQD NSDIKVVPRR KAKIIRDYGK QMAGDGCVAG RQDED.
A SE SE889
           GE.GAVVIQD QSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
A SE UGSE8
           GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGDDCVAG RQDED.
A UG 92UG0
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCMAG RQDED.
A_UG_U455_
           GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED.
AC_IN_2130
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
AC RW 92RW
           GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGDDCVAG RQDED.
AC SE SE94
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDEDW
ACD SE SE8
ACG_BE_VI1
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDGCVAG RQDED.
           GE.GAVVIQD NSEIKVVPRR KVKIIRDYGK QMAGDDCVAS RQDED.
AD SE SE69
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
AD SE SE71
           GE.GAVVIQD NGDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
ADHK NO 97
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG GQDED.
ADK_CD_MAL
           GE.GAVAIQD NNEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
AG BE VI11
           GE.GAVVIQD NSEIKVVPRR KVKIIKDYGK QMAGGDCVAG RQDED.
AG_NG_92NG
AGHU_GA_VI
           GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
AGU_CD_Z32
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
           GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
AJ_BW_BW21
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B_AU_VH_AF
           GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGDDCVAS RQDED.
B CN RL42
           GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
B_DE_D31_U
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMGSDDCVAS RQDED.
B DE HAN U
B FR HXB2_
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B GA OYI__
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B GB_CAM1_
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B GB GB8 A
           GE.GAVVIQD NSEIKVVPRR KVKIIRDYGK QMAGDDCVAG RQDED.
B GB MANC
B_KR_WK_AF
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
           GE.GAVVIOD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B NL 3202A
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
B TW TWCYS
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B US BC LO
B US DH123
           GE.GAVVIQD KSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B US JRCSF
           GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGDDCVAS RQDED.
            GE.GAVVIQD NNDIKVVPRR KAKVIRDYGK QTAGDDCVAS RQDED.
B US MNCG
            GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B US P896
B US_RF_M1
            GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B_US_SF2_K
            GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
            GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B_US_WEAU1
            GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
B_US_WR27_
B_US_YU2_M
            GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
            GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGGDCVAG RQDED.
BF1 BR 93B
            GE.GAVVLQD NSDIKVVPRR KVKIIKDYGK QMAGADCMAS RQDED.
C_BR_92BR0
           GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGADCVAG RQDED.
C_BW_96BW0
           GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGADCVAG RQDED.
C_BW_96BW1
           GE.GAVVIQD NSDIKVVPRR KVKIIKDYGK QMAGADCVAG RQDED.
C_BW_96BW1
C_BW_96BW1
           GEGAVVVIOD NSDIKVVPRR KVKIIRDYGK QMAGADCVAG RQDED.
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAG RQDED.
C_ET_ETH22
           GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED.
C_IN_93IN1
C IN 93IN9 GE.GAVVLQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED.
C_IN_93IN9 GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGADCVAG RQDED.
           GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED.
C_IN_94IN1
C_IN_95IN2
           GE.GAVVIQD NSDIKVVPRR KAKIIKDYGK QMAGADCVAG RQDED.
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDEN.
CRF01 AE C
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQNED.
CRF01 AE C
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF01_AE_C
CRF01_AE_T GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF01_AE_T GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
CRF01 AE T GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
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GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF01 AE_T
CRF01 AE T
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF01 AE T
           GE.GAVVIQD KSDIKVVPRR KAKIIKDYGK QMAGDDCVAG RQDED.
CRF02_AG_F
CRF02 AG F
           GE.GAVVIOD KSDIKVVPRR KAKIIKDYGK QMAGDDCVAG RQDED.
CRF02 AG G GE.GAVVIQD NSDIKVVPRR KAKILRDYGK QMAGDDCVAG RQDED.
CRF02 AG N GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
           GE.GAVVIQD NSDIKVVPRR KVKIVRDYGK QMAGDDCVAG RQDED.
CRF02_AG_S
CRF02 AG S GE.GAVVIQD NSDIKVVPRR KTKILRDYGK QMAGDDCVAG GQNED.
CRF03_AB_R GE.GAVVIQD NNDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
CRF03 AB R GE.GAVVIQD NNDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
CRF04_cpx_
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGNDCVAG RQDED.
CRF04_cpx_
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
           GE.GAVVIQD NSDIKVVPRK KAKIIRDYGK QMAGDDCVAG RQDED.
CRF04_cpx_ GE.GAVVIQD NSDIKVVPRK KAKIIRDYGK QMAGDDCVAG RQDED.
CRF05_DF_B GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF05_DF_B GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF06_cpx_
           GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF06_cpx_
           GE.GAVVIQD NSEIKVVPRR KAKIIKDYGK QMAGDDCVAG RQDED.
CRF06_cpx_
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF06_cpx_ GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
CRF11_cpx_
CRF11_cpx_
           GE.GAIVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAG SQDED.
           GE.GAVVIQD NSDIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
D CD 84ZR0
D_CD_ELI_K GE.GAVVIQD KSDIKVVPRR KVKIIRDYGK QMAGDDCVAS RQDED.
D_CD_NDK_M GE.GAVVIQD NSDIKVVPRR KVKIIRDYGK QMAGDDCVAS RQDED.
D UG 94UG1
           GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDED.
F1 BE V185 GE.GAVVIQD NSEIKIVPRR KAKIIRDYGK QMAVDDCVAG RQDED.
F1 BR 93BR GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
F1 FI FIN9 GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
F1 FR MP41 GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
F2 CM MP25 GE.GAVVIQD NNEIKVIPRR KAKIIRDYGK QMAGDDCVAG RQDED.
F2KU BE VI GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
G BE DRCBL GE.GAVVIQD NNEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
           GE.GAVVIQD NNEIKVVPRR KAKILKDYGK QMAGGDCVAG RQDED.
G NG 92NG0
           GE.GAVVIQD NNEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
G SE SE616
           GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
H BE VI991
H BE VI997
           GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
H_CF_90CF0
           GE.GAVVIQD NSEIKVVPRR EAKIIRDYGK QMAGDDCVAS RQDED.
            GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
J_SE_SE702
           GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
J_SE_SE788
            GE.GAVVIN. .SEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
K_CD_EQTB1
            GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAG RQDED.
K_CM_MP535
N_CM_YBF30
           GE.GAVVIQD NGDIKVVPRR KAKIIRDYGK QMAGDGCVAS GQDENQ
O_CM_ANT70
            GE.GAVVIQD KGDIKVVPRR KAKIIREYGK QMAGTDSMAS GQTESE
            GE.GAVVIQD KGDIKVVPRR KAKIIRDYGK QMAGTDSMAN RQTESE
O CM MVP51
O_SN_99SE_
            GE.GAVVIQD KGDIKVVPRR KAKIIRHYGK QMAGTDSMAS GQTESE
            GE.GAVVIQD KGDIKVVPRR KAKIIRHYGK QMAGTDSMAS GQTESE
O_SN_99SE_
U_CD___83C GE.GAVVIQD NSEIKVVPRR KAKIIRDYGK QMAGDDCVAS RQDEN.
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Table 15. HIV Rev Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

Name:	00000762 1	SEQ ID NO: 970	Len: 129	Check:	4903	Weight:	1.00
-	_ .			Check:		Weight:	1.00
Name:				Check:		Weight:	1.00
Name:	_			Check:		Weight:	1.00
	00BW1471_2			Check:		_	1.00
	00BW1616_2		Len: 129			Weight:	
Name:			Len: 129	Check:		Weight:	1.00
Name:	_		Len: 129	Check:		Weight:	1.00
Name:	_		Len: 129	Check:		Weight:	1.00
	00BW1783_5		Len: 129	Check:		Weight:	1.00
Name:	00BW1795_6		Len: 129	Check:		Weight:	1.00
Name:	00BW1811_3			Check:		Weight:	1.00
	00BW1859_5	SEQ ID NO: 981		Check:		Weight:	1.00
Name:	00BW1880_2	SEQ ID NO: 982	Len: 129	Check:		Weight:	1.00
Name:	00BW1921_1	SEQ ID NO: 983	Len: 129	Check:	6482	Weight:	1.00
Name:	00BW2036_1	SEQ ID NO: 984	Len: 129	Check:	4770	Weight:	1.00
Name:	00BW2063_6	SEQ ID NO: 985	Len: 129	Check:	5384	Weight:	1.00
Name:	00BW2087 2	SEQ ID NO: 986	Len: 129	Check:	4848	Weight:	1.00
Name:	00BW2127_2	SEQ ID NO: 987	Len: 129	Check:	5783	Weight:	1.00
Name:	00BW2276 7	SEQ ID NO: 988	Len: 129	Check:	5364	Weight:	1.00
Name:	00BW3819 3	SEQ ID NO: 989	Len: 129	Check:	5712	Weight:	1.00
Name:	00BW3842 8	SEQ ID NO: 990	Len: 129	Check:	5586	Weight:	1.00
Name:	00BW3871 3	SEQ ID NO: 991	Len: 129	Check:	5299	Weight:	1.00
Name:	00BW3876 9	SEQ ID NO: 992	Len: 129	Check:	4423	Weight:	1.00
	00BW3886 8		Len: 129	Check:	5415	Weight:	1.00
Name:	-	SEQ ID NO: 994	Len: 129	Check:	5426	Weight:	1.00
Name:	00BW3970 2	SEQ ID NO: 995	Len: 129	Check:		Weight:	1.00
Name:	-			Check:		Weight:	1.00
Name:	_ _		Len: 129	Check:		Weight:	1.00
Name:		SEQ ID NO: 998	Len: 129	Check:		Weight:	1.00
Name:			Len: 129	Check:		Weight:	1.00
	96BW06 J4		0 Len:129	Check:		Weight:	1.00
Name:	-		1 Len:129	Check:		Weight:	1.00
Name:			2 Len:129	Check:		Weight:	1.00
			2 Len:129	Check:		Weight:	1.00
Name:			4 Len:129	Check:		Weight:	1.00
Name:	_		5 Len:129	Check:		Weight:	1.00
Name:	96BW17A09					Weight:	
	96BWMO1_5		6 Len:129	Check:		_	1.00
	96BWMO3_2		7 Len:129	Check:		Weight:	1.00
	98BWMC12_2		8 Len:129	Check:		Weight:	1.00
Name:			9 Len:129	Check:		Weight:	1.00
Name:			0 Len:129	Check:		Weight:	1.00
		SEQ ID NO: 101		Check:		Weight:	1.00
		SEQ ID NO: 101		Check:		Weight:	1.00
	98BWMO36_a		_	Check:		Weight:	1.00
		SEQ ID NO: 101		Check:		Weight:	1.00
		SEQ ID NO: 101	5 Len:129	Check:		Weight:	1.00
	99BW4642_4			Check:		Weight:	1.00
	99BW4745_8		<u>7</u> Len:129	Check:		Weight:	1.00
	99BW4754_7			Check:		Weight:	1.00
	99BWMC16_8			Check:		Weight:	1.00
	A2_CD_97CD			Check:		Weight:	1.00
	A2_CY_94CY		<u>1</u> Len:129	Check:		Weight:	1.00
Name:	A2D97KR		2 Len:129	Check:		Weight:	1.00
Name:	A2G_CD_97C			Check:		Weight:	1.00
	A_BY_97BL0		<u>4</u> Len:129	Check:		Weight:	1.00
Name:	A_KE_Q23_A	SEQ ID NO: 102	<u>5</u> Len:129	Check:	2684	Weight:	1.00

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Weight:
                                                                   1.00
Name: A SE SE659 SEQ ID NO: 1026 Len:129
                                           Check: 4659
                                                                   1.00
Name: A SE SE725 SEQ ID NO: 1027 Len:129
                                           Check: 4491
                                                         Weight:
                                                                   1.00
Name: A SE SE753 SEQ ID NO: 1028 Len:129
                                           Check: 3636
                                                         Weight:
                                                                   1.00
Name: A SE SE853 SEQ ID NO: 1029 Len:129
                                           Check: 1862
                                                         Weight:
                                                                   1.00
                                           Check: 2798
                                                         Weight:
Name: A SE SE889 SEQ ID NO: 1030 Len:129
Name: A_SE_UGSE8 SEQ ID NO: 1031 Len:129
                                                         Weight:
                                                                   1.00
                                           Check: 6865
                                                         Weight:
                                                                   1.00
Name: A UG 92UG0 SEQ ID NO: 1032 Len:129
                                           Check: 4427
                                                                   1.00
Name: A UG U455 SEQ ID NO: 1033 Len:129
                                           Check: 3229
                                                         Weight:
Name: AC IN 2130 SEQ ID NO: 1034 Len:129
                                           Check: 5110
                                                         Weight:
                                                                   1.00
                                           Check: 5015
Name: AC RW 92RW SEQ ID NO:
                            1035 Len:129
                                                         Weight:
                                                                   1.00
                                           Check: 7976
Name: AC SE SE94 SEQ ID NO: 1036 Len:129
                                                         Weight:
                                                                   1.00
                                           Check: 2296
Name: ACD_SE_SE8 SEQ ID NO: 1037 Len:129
                                                         Weight:
                                                                   1.00
                                           Check: 3968
                                                         Weight:
                                                                   1.00
Name: ACG BE VI1 SEQ ID NO: 1038 Len:129
                                                         Weight:
                                                                   1.00
Name: AD_SE_SE69 SEQ ID NO: 1039 Len:129
                                           Check: 4558
                        NO: 1040 Len:129
                                           Check: 2678
                                                         Weight:
                                                                   1.00
Name: AD SE SE71 SEQ ID
                                           Check: 1890
                                                         Weight:
                                                                   1.00
Name: ADHK NO_97 SEQ_ID
                        NO: 1041 Len:129
Name: ADK CD MAL SEQ ID
                        NO: 1042 Len:129
                                           Check: 5260
                                                         Weight:
                                                                   1.00
                        NO: 1043 Len:129
Name: AG_BE_VI11 SEQ ID
                                           Check: 4003
                                                         Weight:
                                                                   1.00
                                           Check: 5027
                                                         Weight:
                                                                   1.00
Name: AG_NG_92NG SEQ ID
                        NO: 1044 Len:129
                                           Check: 1978
                                                         Weight:
                                                                   1.00
Name: AGHU GA_VI SEQ ID
                        NO: 1045 Len:129
Name: AGU_CD_Z32 SEQ ID
                        NO: 1046 Len:129
                                           Check: 1958
                                                         Weight:
                                                                   1.00
                        NO: 1047 Len:129
                                           Check: 2263
                                                         Weight:
                                                                   1.00
Name: AJ BW BW21 SEQ ID
Name: B_AU_VH_AF SEQ_ID
                        NO: 1048 Len:129
                                           Check: 4074
                                                         Weight:
                                                                   1.00
                        NO: 1049 Len:129
                                           Check: 4483
                                                         Weight:
                                                                   1.00
Name: B CN_RL42_ SEQ ID
                                           Check: 5079
Name: B_DE_D31_U SEQ ID
                        NO: 1050 Len:129
                                                         Weight:
                                                                   1.00
                                                         Weight:
                                                                   1.00
Name: B_DE_HAN_U SEQ ID
                        NO: 1051 Len:129
                                           Check: 4550
                                           Check: 3649
                                                                   1.00
                        NO: 1052 Len:129
                                                         Weight:
Name: B FR HXB2 SEQ ID
                                                                   1.00
                                           Check: 3334
                                                         Weight:
Name: B GA OYI M SEQ ID
                        NO: 1053 Len:129
                                                         Weight:
                                                                   1.00
Name: B GB CAM1 SEQ ID
                        NO: 1054 Len:129
                                           Check: 3865
                                                                   1.00
                        NO: 1055 Len:129
                                           Check: 3083
                                                         Weight:
Name: B GB GB8 A SEQ ID
                        NO: 1056 Len:129
                                           Check: 5502
                                                         Weight:
                                                                   1.00
Name: B GB MANC SEQ ID
Name: B KR WK AF SEQ ID
                                           Check: 4156
                                                         Weight:
                                                                   1.00
                        NO: 1057 Len:129
Name: B NL 3202A SEQ ID
                        NO: 1058 Len:129
                                           Check: 3826
                                                         Weight:
                                                                   1.00
                                           Check: 3546
                                                         Weight:
                                                                   1.00
Name: B TW TWCYS SEQ ID
                        NO: 1059 Len:129
                                           Check: 4674
                                                         Weight:
                                                                   1.00
Name: B US BC LO SEQ ID
                        NO: 1060 Len:129
                                           Check: 4202
                                                                   1.00
Name: B US DH123 SEQ ID
                        NO: 1061 Len:129
                                                         Weight:
Name: B US JRCSF SEQ ID
                        NO: 1062 Len:129
                                           Check: 3217
                                                         Weight:
                                                                   1.00
Name: B_US_MNCG_ SEQ ID
                        NO: 1063 Len:129
                                           Check: 3512
                                                         Weight:
                                                                   1.00
SEQ ID
                        NO: 1064 Len:129
                                           Check: 3297
                                                         Weight:
                                                                   1.00
                                           Check: 5527
                                                         Weight:
                                                                   1.00
Name: B US SF2 K SEQ ID NO: 1066 Len:129
                                           Check: 3616
                                                         Weight:
                                                                   1.00
Name: B_US_WEAU1 SEQ ID NO: 1067 Len:129
                                           Check: 4435
                                                         Weight:
                                                                   1.00
Name: B_US_WR27_ SEQ ID NO: 1068 Len:129
                                           Check: 812
                                                         Weight:
                                                                   1.00
Name: B_US_YU2_M SEQ ID NO: 1069 Len:129
                                           Check: 4948
                                                         Weight:
                                                                   1.00
Name: BF1_BR_93B <u>SEQ ID NO: 1070</u> Len:129
                                           Check: 3645
                                                         Weight:
                                                                    1.00
Name: C_BR_92BR0 <u>SEQ ID NO: 1071</u> Len:129
                                                         Weight:
                                                                    1.00
                                           Check: 4262
Name: C_BW_96BW0 <u>SEQ ID NO: 1072</u> Len:129
                                           Check: 4323
                                                         Weight:
                                                                    1.00
Name: C_BW_96BW1 SEQ ID NO: 1073 Len:129
                                           Check: 3054
                                                         Weight:
                                                                    1.00
Name: C_BW_96BW1 SEQ ID NO: 1074 Len:129
                                           Check: 3900
                                                         Weight:
                                                                    1.00
                                           Check: 4051
                                                         Weight:
                                                                    1.00
Name: C_BW_96BW1 SEQ ID NO: 1075 Len:129
Name: C_ET_ETH22 SEQ ID NO: 1076 Len:129
                                           Check: 3843
                                                         Weight:
                                                                    1.00
Name: C_IN_93IN1 <u>SEQ ID NO: 1077</u> Len:129
                                           Check: 2878
                                                         Weight:
                                                                    1.00
Name: C_IN_93IN9 <u>SEQ ID NO: 1078</u> Len:129
                                           Check: 4499
                                                         Weight:
                                                                    1.00
Name: C_IN_93IN9 <u>SEQ ID NO: 1079</u> Len:129
                                           Check: 3994
                                                         Weight:
                                                                    1.00
Name: C_IN_94IN1 SEQ_ID_NO: 1080 Len:129
                                           Check: 4362
                                                         Weight:
                                                                    1.00
                                           Check: 3765
                                                         Weight:
                                                                    1.00
Name: C_IN_95IN2 SEQ ID NO: 1081 Len:129
                                           Check: 4444
                                                         Weight:
                                                                    1.00
Name: CRF01_AE_C SEQ ID NO: 1082 Len:129
                                           Check: 3760
                                                         Weight:
                                                                    1.00
Name: CRF01_AE_C SEQ ID NO: 1083 Len:129
Name: CRF01_AE_C SEQ ID NO: 1084 Len:129
                                           Check: 3562
                                                         Weight:
                                                                    1.00
Name: CRF01_AE_T SEQ ID NO: 1085 Len:129
                                           Check: 5676
                                                         Weight:
                                                                    1.00
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Check: 6090
                                                         Weight:
                                                                    1.00
Name: CRF01 AE T SEQ ID NO: 1086 Len:129
Name: CRF01_AE_T SEQ ID NO: 1087 Len:129
                                            Check: 6846
                                                         Weight:
                                                                    1.00
Name: CRF01 AE T SEQ ID NO: 1088 Len:129
                                            Check: 5393
                                                         Weight:
                                                                    1.00
                                                                    1.00
Name: CRF01 AE T SEQ ID NO: 1089 Len:129
                                            Check: 6189
                                                         Weight:
Name: CRF01 AE T SEQ ID NO: 1090 Len:129
                                            Check: 5202
                                                          Weight:
                                                                    1.00
                                            Check: 5063
                                                         Weight:
                                                                    1.00
Name: CRF02 AG F SEQ ID NO: 1091 Len:129
                                                                    1.00
Name: CRF02 AG F SEQ ID NO: 1092 Len:129
                                            Check: 3731
                                                          Weight:
Name: CRF02 AG G SEQ ID NO: 1093 Len:129
                                            Check: 2202
                                                          Weight:
                                                                    1.00
Name: CRF02 AG N SEQ ID NO: 1094 Len:129
                                            Check: 4873
                                                          Weight:
                                                                    1.00
                                            Check: 3995
                                                          Weight:
Name: CRF02 AG S SEQ ID NO: 1095 Len:129
                                                                    1.00
                                            Check: 6502
Name: CRF02 AG S SEQ ID NO: 1096 Len:129
                                                          Weight:
                                                                    1.00
Name: CRF03_AB_R SEQ ID NO: 1097 Len:129
                                            Check: 2858
                                                          Weight:
                                                                    1.00
Name: CRF03_AB_R SEQ ID NO: 1098 Len:129
                                                                    1.00
                                            Check: 2808
                                                          Weight:
                      ID NO: 1099 Len:129
                                            Check: 3912
                                                                    1.00
                                                          Weight:
Name: CRF04_cpx_ <u>SEQ</u>
Name: CRF04 cpx SEQ ID NO: 1100 Len:129
                                            Check: 3700
                                                          Weight:
                                                                    1.00
Name: CRF04_cpx_ SEQ ID NO: 1101 Len:129
                                            Check: 3297
                                                                    1.00
                                                          Weight:
Name: CRF05_DF_B SEQ ID NO: 1102 Len:129
                                            Check: 3974
                                                          Weight:
                                                                    1.00
Name: CRF05_DF_B SEQ ID NO: 1103 Len:129
                                            Check: 4062
                                                          Weight:
                                                                    1.00
                                            Check: 2954
                                                          Weight:
                                                                    1.00
Name: CRF06_cpx_ <u>SEQ</u>
                      ID NO: 1104 Len:129
Name: CRF06_cpx_ SEQ ID NO: 1105 Len:129
                                                          Weight:
                                                                    1.00
                                            Check: 1655
Name: CRF06_cpx_ SEQ ID NO: 1106 Len:129
                                            Check: 2327
                                                          Weight:
                                                                    1.00
                                            Check: 2706
                                                          Weight:
                                                                    1.00
Name: CRF06_cpx_ SEQ ID NO: 1107 Len:129
Name: CRF11_cpx_ SEQ ID NO: 1108 Len:129
                                            Check: 2064
                                                          Weight:
                                                                    1.00
Name: CRF11_cpx_ SEQ ID NO: 1109 Len:129
                                                          Weight:
                                                                    1.00
                                            Check: 1685
Name: D_CD_84ZR0 <u>SEQ ID NO: 1110</u> Len:129
                                            Check: 4305
                                                          Weight:
                                                                    1.00
                                            Check: 4483
                                                                    1.00
Name: D CD ELI K SEQ ID NO: 1111 Len:129
                                                          Weight:
                                                                    1.00
Name: D CD NDK M SEQ ID NO: 1112 Len:129
                                            Check: 3024
                                                          Weight:
                                                          Weight:
                                                                    1.00
Name: D UG 94UG1 SEQ ID
                         NO:
                             1113 Len:129
                                            Check: 3298
                                                                    1.00
Name: F1 BE VI85 SEQ ID
                             1114 Len:129
                                            Check: 2602
                                                          Weight:
                         NO:
                                            Check: 2572
                                                          Weight:
                                                                    1.00
Name: F1 BR 93BR SEQ ID
                         NO: 1115 Len:129
                                            Check: 3253
                                                          Weight:
                                                                    1.00
Name: F1 FI FIN9 SEQ ID
                         NO: 1116 Len:129
                                            Check: 2465
                                                          Weight:
                                                                    1.00
Name: F1 FR MP41 SEQ ID
                         NO: 1117 Len:129
Name: F2 CM MP25 SEQ
                      ID
                         NO: 1118 Len:129
                                            Check: 2231
                                                          Weight:
                                                                    1.00
                         NO: 1119 Len:129
                                                                    1.00
Name: F2KU BE VI SEQ
                      ID
                                            Check: 461
                                                          Weight:
                      ID
                         NO: 1120 Len:129
                                            Check: 3194
                                                          Weight:
                                                                    1.00
Name: G BE DRCBL SEQ
                         NO: 1121 Len:129
Name: G NG 92NG0 SEQ
                                            Check: 4325
                                                          Weight:
                                                                    1.00
                      ID
                                            Check: 2614
                                                          Weight:
                                                                    1.00
Name: G SE SE616 SEQ
                      ID
                         NO: 1122 Len:129
                                            Check: 2347
                                                          Weight:
                                                                    1.00
Name: H BE VI991 SEQ
                      ID
                         NO: 1123 Len:129
                                            Check: 1680
                                                          Weight:
Name: H BE VI997 SEQ
                         NO: 1124 Len:129
                                                                    1.00
                      ID
Name: H_CF_90CF0 SEQ
                                                          Weight:
                                                                    1.00
                         NO: 1125 Len:129
                                            Check: 2751
                      ID
Name: J_SE_SE702 SEQ
                                            Check: 2099
                                                          Weight:
                                                                    1.00
                      ID
                         NO: 1126 Len:129
                         NO: 1127 Len:129
                                            Check: 2149
                                                          Weight:
                                                                    1.00
Name: J_SE_SE788 SEQ
                      ID
                                            Check: 3510
                                                          Weight:
                                                                    1.00
Name: K_CD_EQTB1 SEQ
                      ID
                         NO: 1128 Len:129
                                            Check: 2798
Name: K_CM_MP535 SEQ ID
                         NO:
                             1129 Len:129
                                                          Weight:
                                                                    1.00
                         NO: 1130 Len:129
Name: N_CM_YBF30 SEQ ID
                                            Check: 3973
                                                          Weight:
                                                                    1.00
Name: O_CM_ANT70 SEQ ID
                         NO: 1131 Len:129
                                            Check: 9677
                                                          Weight:
                                                                    1.00
Name: O_CM_MVP51 SEQ ID
                                            Check: 8852
                                                          Weight:
                                                                    1.00
                         NO: 1132 Len:129
Name: O_SN_MP129 SEQ ID NO: 1133 Len:129
                                            Check: 1678
                                                          Weight:
                                                                    1.00
                                            Check: 2242
                                                          Weight:
                                                                     1.00
Name: O_SN_MP130 SEQ_ID_NO: 1134 Len:129
Name: U_CD___83C SEQ ID NO: 1135 Len:129
                                                          Weight:
                                                                     1.00
                                            Check: 9312
                                                                              50
SEQ ID NO
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                       MAGRSGD... NDDTLLQAVR IIKILYQSNP YPK.PEGTRQ ARRNRRRRWR
970
           00BW0768 2
                        MAGRSEDS.. .DATLLQAVR IIKILYQSNP YPK.PEGTRQ ARKNRRRRRR
971
                        MAGRSGD... SDEALLQAVR IIKVLYQSNP YPK.PEGTRQ ARKNRRRRWR
           00BW0874 2
972
                        MAGRSGD... SDEALLQAVR IIRILYQSNP YPKPEG.TRQ ARKNRRRRWR
           00BW1471 2
973
                        MAGRSGDS...DEALLQAVR TIKILYQSNP YPE.PKGTRQ ARKNRRRRWR
           00BW1616 2
974
                        MAGRSGDS...DEALLQAIK SIKILYQSNP YPE.PQGTRQ AQRNRRRRWR
           00BW1686 8
975
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00BW1759 3
                       MAGRSGD... NDEAVLQAIR IIKILYQSNP YPK.PRGTRQ AQKNRRRRWR
976
977
           00BW1773 2
                       MAGRSGDS....DEALLQAVK IIKILYQSNP YPE.PKGTRQ ARKNRRRRWR
                       MAGRSGD... SDEAVLOAVR IIKILYQSNP YPK.PEGTRQ ARKNRRRRWR
           00BW1783 5
978
                       MAGRSGD... GDAALLQAVR IIKILYQSNP YPK.PEGTRQ ARKNRRRRWR
           00BW1795 6
979
           00BW1811 3
                       MAGRSGD... SDEELLQVAR IIKILYQSNP YPE.PRGTRQ ARKNRRRRWR
980
           00BW1859 5
                       MAGRSEDS.. .DAALLQAAK IIKIIYQSNP YPE.PKGTRQ ARRNRRRRWR
981
           00BW1880 2
                       MAGRSGD... NDEALLOAVR IIKILYOSNP FPK.PEGTRQ ARKNRRRRWR
982
           00BW1921 1
                       MAGRSGD... NDEALLQAVR IIKILYQSNP YPE.PQGTRQ ARKNRRRRWR
983
                       MAGRSEDS.. . DEALLQAIR LIKILYQSNP YPE.PKGTRQ ARKNRRRRWR
           00BW2036 1
984
                       MAGRSGDN.D ADAALLOAVK IIKILYOSNP YPK.PEGTRQ ARKNRRRRWR
           00BW2063 6
985
           00BW2087 2
                       MAGRSGD... SDEALLQAVR IIKILYQSNP YPK.PEGTRQ ARKNRRRRWR
986
                       MAGRSGD... NDEARLQVVK IIKILYQSNP YPK.PEGTRQ ARKNRRRRWR
           00BW2127 2
987
           00BW2276 7
                       MAGRSGD... SDEALLQAVR IIKIIYQSNP YPK.PEGTRQ ARRNRRRRWK
988
                       MAGRSGD... SDEDLLKAVR LIKILYQSNP YPK.PEGTRR AQRNRRRRWR
           00BW3819 3
989
                       MAGRSEDS.. .DEALLRVVR IIKILYQSNP YPE.PKGTRQ ARKNRRRRWR
           00BW3842 8
990
                       MAGRSGDS....DEALLQAIR TIKILYQSNP YPE.PKGTRQ ARKNRRRRWR
           00BW3871 3
991
992
           00BW3876 9
                       MAGRSGDS....DEALLHAVR TIKILYXSNP YPE.PKGTRQ ARKNRKRRWR
                       MAGRSGDS...DEALLQAVR IIKILYQSNP YPE.HQGTRQ ARKNRRRRWG
993
           00BW3886 8
                       MAGRSGDS....DEALLQAVR IIKILYQSNP YPK.PEGTRQ ARKNRRRRWR
           00BW3891 6
994
                       MAGRSGDS....DEALLOAVK IIKILYOSDP YPK.PEGTRQ ARKNRRRRWR
995
           00BW3970 2
                       MAGRSGDN...DEALLQAVR IIKILYQSNP YPK.PEGTRQ ARKNRRRRWR
           00BW5031 1
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                       MAGRSGD... SDEALLOAVR IIRILYQSNP YPE.PRGTRR ARKNRRRRWR
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                       MAGRSGD... SDEALLQAVK IIKILYQSNP YPK.PEEIRQ ARKNRRRRWR
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             96BW0407
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             96BW0502
                       MAGRSGDS....DEALLQAVR IIKILYQSNP SPE.PKGNRQ ARKNRRRRWR
1000
            96BW06_J4
            96BW11 06
                       MAGRSGD... NDEALLQAVR IIKILYQSNP YPK.PEGTRQ ARKNRRGRWR
1001
                       MAGRSGD... SDEALLQAVR IIKILYQNNP YPK.PEGTRQ ARKNRRRRWR
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1002
                       MAGRSEDS.. .DEALLHAVR IIKILYQSNP YPE.PKGTRQ ARKNRRRRWR
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            96BW15B03
            96BW16 26
                       MAGRSGDS....DAALLQAVR IIKILYQSNP YPK.PKGTRQ ARKNRRRRWR
1004
                       MAGRSGD... NDEALLOAMG IIKILYOSNP YPKPEG.TRR ARKNRRRRWR
1005
            96BW17A09
                       MAGRSGD... SDEALLQAVR IIKILYQSNP YPK.PEGTRQ ARRNRRRRWR
            96BWM01 5
1006
            96BWMO3 2
                       MAGRSGD... SDEALLQAVR TIKILYQSNP YPK.PEGTRQ ARKNRRRRWR
1007
                       MAGRSGDS...DEALLQAVR IIKILYQSNP QPK.PEGTRQ ARKNRRRRWR
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           98BWMC12 2
                       MAGRSGD... SDEALLQAVR IIKILYQSNS YPK.PEGTRQ ARKNRRRRWR
           98BWMC13 4
1009
1010
           98BWMC14 a
                       MAGRSGDS....DEALLQAVR IIKILYQSNP PPE.RRGIGQ ARXNRRRRWR
                       MAGRSGD... DDERLLQAVR IIKILYQSNP YPS.PEGTRQ ARRNRRRRWR
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1011
                       MAGRSGD... SDEALLQAVR IIKILYQSNP YPK.PEGTRQ ARKNRRRRWR
           98BWM018 d
1012
                       MAGRSGV... SDEALLQAVK IIKILYQSNP YPNNPEGSRQ AQRNRRRRWR
1013
           98BWM036 a
                       MAGRSGD... SDEALLQAVR IIKILYQSNR YPK.PEGTRQ AQRNRRRRWR
           98BWM037 d
1014
                       MAGRSGD... PDEALLQAIR IIKILYQSNP YPK.PEGTRQ ARRNRRRRWR
1015
           99BW3932 1
                       MAGRSEDSG. .DAALLQAVR IIKILYQSNP YPE.PKGTRQ ARKNRRRRWR
           99BW4642 4
1016
                       MAGRSGDS....DEALLQAVR IIKILYQSNP YPK.PKETRQ ARRNRRRRWR
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           99BWMC16 8
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           A2 CY 94CY
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           A2D 97KR
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            RRQWWIQSLS GWILNTHLGR PAEPVPLQLP PLERLTLDCN EECGTSGTQG
B_KR_WK_AF
B NL 3202A ERQRQIRSIS ERILSTYLGR SAEPVPLQLP PLERLTLDCD EDCGTSGTQG
B TW TWCYS ERQRQIRTIS GWILSNYLGR PAEPVPLQLP PLERLTLDCD EDCGTSGTQG
B_US_BC_LO ERQRQIRSIS ERILSTFLGR SAEPVPLQLP PLERLNLGCN EDCGTSGTQG
B US DH123 QRQRQIQSIS GWILSNHLGR PADAVPLQLP PLERLTLDCN EDCGTSGTQG
B_US_JRCSF ERQRQIRTIS ERILSTYLGR PAEPVPLQLP PLERLTLDCN EDCGTSGTQG
            ERQRHIRSIS AWILSNYLGR PAEPVPLQLP P.QRLTLDCS EDCGTSGTQG
B_US_MNCG_
```

ERQRQIRSIS ERILGTFLGR FEEPVPLPLP PLEKLTLDCN EDCGTSGTQG B_US_P896 ERQRQIRRCS EWILDTYLGR SVDPVQLQLP PLERLTLDSS EDCGTSGTQG B US RF M1 B US_SF2_K ERQRQIRSIS GWILSTYLGR SAEPVPLQLP PLERLTLDCS EDCGNSGAQG ERQRQIRKIS GWILNTYLGR PTEPVPLPLP PLDRLTLDCK EDCGTSGTQG B US WEAU1 .RQRQIQSLS AWIISTHLGR PAEPVPLQLP PLERLTLDCS EDCGTSGTQG B_US_WR27_ ERQRQIRSIS GWLLSNYLGR PTEPVPFQLP PLERLTLDCN EDCGTSGTQG B US YU2 M ARQRQIREIS ERILSSCLGR PEEPVPLQLP PLERLHINCS EDCGQGTEEG BF1 BR 93B ARORQIHSIS ERILSTCVGR PAEPVPFQLP PIERLNINCS ESGGTSGTQQ C BR_92BR0 ARQRQIHSIS ERILSTCLGR PTEPVPLQLP PIERLHIDCS ESSGASGTQQ C_BW_96BW0 ARQKQINSIS ERILSTCLGR SAEPVPFLLP PIERLHISDS ESGGTSGTQQ C_BW_96BW1 C_BW_96BW1 ARQRQIHSIS ERILSTCLGR PAEPVPLQLP PIERLHIGGS ENSGTTGTQQ AROROIDSIS TRILSTCLGR PEEPVPFQLP PIERLNIGDS ESGGTSGTQQ C_BW_96BW1 C_ET_ETH22 ARQRQIHTLS ERILSNFLGR PAEPVPLQLP PLERLNLDCS EDSGTSGTQQ ARQRQIHSIS ERILSTCLGR STEPVPLQLP PIERLHIGGS ESGGTSGTQQ C_IN_93IN1 ARQRQIHSLS ERILSACLGR PAEPVPLQLP PLERLHISGS ESGGTSGTQQ C IN 93IN9 ARQKQIHSLS ERILSTCLGR SAEPVPLQLP PLERLHISGS ESGGTSGTQQ C_IN_93IN9 ARQRQIHSIS ERILSACLGR PAEPVPLQLP PIERLHISGS ESGGTSGTQQ C IN 94IN1 C_IN_95IN2 ARQRQIHSIS ERILSTFLGR PAEPVPLQLP PIERLHISGS ESAGTSGTPQ CRF01_AE_C RRQRQIHSLS ERILVACVGR STEPVPLQLP PLERLHIDCS EDCGTSGTQQ CRF01_AE_C ARQRQIHKIG ERILSTCLGR SPEPVPLQLP PLERLHLDCS EDCGTSGTQQ CRF01_AE_C ARQRQIRALS ERILSACLGR SAEPVPLQLP PLERLHLDCS EDCGTSGTQQ CRF01_AE_T ARQRQIRAIS ERILITCLGR STEPVPLQLP PLERLHLDCN EDCGTSGTQQ CRF01_AE_T ARQRQIRAIS ERILNACVGR STEPVPLQLP PLERLHLDCS EDCGTSGTQQ CRF01_AE_T ARQRQIRAIS ERILSTCLGR STEPVPLQLP PLERLHLDCS EDCGTSGTQQ CRF01 AE T ARQRQIREIS ERILSSCVGR STEPVPLPLP PLERLHLDCS EDCGTSGTQQ CRF01_AE_T ARQRQISAIS ERILSTCLGR STEPVPLQLP PVERLNLDCS EDGGTSGTQQ CRF01_AE_T ARQRQISAIS ERILSACLGR STEPVSLPLP PLERLHLDCS EDCGTSGTQQ ARQRQIRAIS ERFLSTCLGR SAEPVPLQLP PIERLCLDCS EGCGTSGTQQ CRF02 AG F CRF02_AG_F ARQRQIRAIS QRILSTCLGR SAEPVPLQLP PLERLCLDCS EGCGTSGTQQ CRF02_AG_G ARQRQIHSLS ERILSTCLGR PEEPVSFQLP PLERLNLDCS EDCGNSGTQS CRF02 AG N ARQRQIRAIS ERILSTCLGR SAEPVPLQLP PIERLNLDCS EDCGTSGTQL ARQRQIRAIS ERILSTCLGR SAEPVPLQLP PIERLRLDCS EDCGTSGTQG CRF02 AG S ARQRQVRAIS ERILSTCLGR PAEPVPLPLP PIERLCLDCS EDSGTSGTQQ CRF02 AG S CRF03 AB R ERQRHIHSIS EQILSTYLGR PEEPVLLHLP PLERLTLDCS EDCGTSGTQG CRF03 AB R ERQRHIHSIS QRILSTYLGR PEEPVPLHLP PLERLTLDCS EDCGTSGTQG AROKOIHSLS ERILATYLGR PAEPVPLQLP PLEKLTLNCS EDCGTSGDKG CRF04_cpx_ ARQKQIHSIS ERVLATYLGR PAEPVPLQLP PLEKLTLNCS EDCGTSGEKG CRF04_cpx_ ARQNRIHSIS ERILAACLGR PAEPVPLQLP PIEKLTLDCS EDCGTSGDKG CRF04_cpx_ CRF05_DF_B ARQRQINSIG ERLLSTYLGR SEEPVPLQLP PLERLNLNCS EDCGTSGTQG CRF05_DF_B ARQRQIRSIA DRIVDTYLGR PEEPVPLQLP PLERLNLNCS EDCGTSGTQG CRF06_cpx_ ARQNQIDSIS ERVLSTCLGR SAEPVPLQLP PIERLRLDCS EDCGNSGTQG CRF06_cpx_ ARQNQIDSIS ERILSTCLGR PTEPVPFQLP PIERLRLDCS EDCGNSGTQG CRF06_cpx_ ARQKQIDSIS ERILSTCLGR SAEPVPLQLP PIERLRLDCS EDCGNSGTQG CRF06_cpx_ ARQNQIDSIS ERILSSCLGR SEEPVPLQLP PIERLRLDCT EDCGNSGTQG CRF11_cpx_ ARQNQIDSIS QRILSDCLGR SEEPVPLQLP PIERLHLDCS EDCGNPGTQG CRF11_cpx_ ARQNQLHSIS QRILSTCLGR SEEPVPLPLP PIERLHLDCS EDCGNSGTQG D CD 84ZRO ARQRYIHSIG ERILSTYLGR SEEPVPLQLP PLERINLNCS EDCGTSGTQG D_CD_ELI_K ARQRQIREIA ERILGTYLGR PAEPVPLQLP PLERLNLNCS EDCRTSGTQG D CD NDK M ARQRQIHSIG ERIICTFLGR PEEPVPLQLP PLERLNLNCS EDCGTSGTQG D UG 94UG1 ARQRQIHSIG ERIISTYLGR FEEPVPLQLP PLERLNLNCS EDCGTSGTQG F1_BE_VI85 ARQRQIRALS DRILSSCLGR SEEPVPLQLP PLERLHINCS EDCGQGPEEG F1_BR_93BR ARQRQIREIS DRILSSCLGR PAEPVPLQLP PLERLHINCS EDCGQGAEEG F1 FI FIN9 ARQRQIRAIS ERILSSCLGR LEEPVPLQLP PLERLHINCS EDCGQGTEEG F1 FR MP41 ARQKQIRSIS ERILVACLGR PEEPVPLQLP PLERLHINCS KDCGQGTNEG F2 CM MP25 ARQRQIHQIS ERILSTCLGR LQEPVRLQLP LLEKLHINCS EDCGQGTEKG F2KU BE VI ARQRQIHSIS QRILSTCLGR PAEPVPFQLP PLERLNLDCS EDSREGAEGE G_BE_DRCBL ARQRQIHSIS ERILSTCLGR PEEPVPLQLP PLERLHLDCS EDGGTSGTQQ G_NG_92NG0 ARQRQIHSIS ERILSACLGR PAEPVPFQLP PLEGLSLDCS KDGGTSGTQQ G SE_SE616 ARQRQISAIS ERILTAYLGR PAEPVPLQLP PLERLHLDCS EDSGTSGTQQ H BE VI991 ARQRQIHSIG ERVLATCLGG PAEPVPLQLP PLERLTLDCS EDCGTSGEKG

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ARQRQIRAIS ERILTDCLGR PPEPVPLQLP PLERLTLDCN KDCGTSGEKG
H BE VI997
H CF 90CF0
         ARORQIREIS ERILTSCLGR PPEPVTLQLP PLERLTLNCS EDCGTSGEKG
J SE SE702
         ARONOIDSIS ERILSSCLGR PAEPVPLQLP PIERLRLDCS EDCGNSGTQG
J SE SE788
         ARONOIDSIS ERIPSSCLGR PAEPVPLQLP PIERLRLDCS EDCGNSGTQG
         ARQRQIREIS QRVLSSCLGR STEPVPLQLP PLERLSLNCD EDSGQGTEGE
K CD EQTB1
         ARQKQISSIS ERLLSACLGR SAEPVPLQLP PIEKLNLNCD EDPGKGTEGG
K CM MP535
         ARQRQIRAIS ERILSSCLGG PPEPVDLPLP PLDRLTLDTE EDSGTPGTES
N CM YBF30
         RRQAQVDTLA ARVLATVVHG PQNNNIVDLP PLEQLSIRDP EGDQLSEAWT
O CM ANT70
         RRQAQVDSLA TRILATVVHG SQDNNLVDLP PLEQLNIRDP EADRLPGTGT
O CM MVP51
         TRHAHVDTLA ARILATVVHG PQDNNLVELP PLEQLSIRDP DGDQPSGTWT
O SN MP129
         KROAOIDTLA ARILATVVHG PQDNNLVELP PLEQLSIRDP DGDQPSGTWT
O SN MP130
         RRQQQIRSIS ERILSTCLGR PAEPVHLQLP PLERLNLDCS ....KGTATG
U_CD___83C
         101
                                129
00BW0762 1
         PQGTPEGMGN P.......
00BW0768_2
         SQGTSEGVGS P.......
         SQGTTEGVGN P......
00BW0874 2
         SQGITEGVGS P......
00BW1471 2
         ....TQGVGS P........
00BW1616 2
         SQGATEGVGN P......
00BW1686_8
00BW1759_3 .....VGS P..... ....
         SQGTTEGVGS P.......
00BW1773_2
00BW1783 5
         SQGTTEGVGN P.......
00BW1795 6
         SQGTPEGVGN P.......
00BW1811_3
         SQGTPEGVGN P.......
00BW1859 5
         SOGTTEGVGS P.......
00BW1880 2
         SQGTPEGVGN P.......
00BW1921 1
         SOGTTEGVGN P.......
00BW2036 1
         SOGTTEGVGS P.......
         SQGTPEGVGN P......
00BW2063 6
         PQGTTEGVGN P......
00BW2087 2
         .....VGS P.......
00BW2127 2
00BW2276_7
         SOGTTEGVGS P.......
00BW3819 3
         SQGTTEGVGS P.......
00BW3842 8
         PQGTTEGVGS P......
00BW3871 3
         SQGTTEGVGN P......
00BW3876 9
         SQGTKEGVGS P.....
00BW3886 8
         SQGTTEGVGS P.......
00BW3891_6
         SQGTTEGVGS P.......
         .....GVGH P.......
00BW3970_2
         PQGDTEGVGR P......
00BW5031 1
 96BW01B21
         SQGTTEGVGN P......
 96BW0407
         SQGTTEGVGN P......
 96BW0502
         ....TEGVGS P......
 96BW06_J4 SQGPTEGVGS P...... .....
         SQGTPEGVGN P.......
 96BW11_06
         SQGTTEGVGS P......
 96BW1210
         SQGTTEGVGS P.....
 96BW15B03
 96BW16 26
         .....GVGS P.......
 96BW17A09 SQGATEGVGS P.......
 96BWMO1 5 SQGTPEGVGN P......
         SQGTTEGVGS S......
 96BWM03 2
         SQGTAEGVGS P.......
98BWMC12 2
         SHGTPEGVGN P......
98BWMC13 4
98BWMC14 a
         ....TOGVGN P......
98BWMO14 1
         SLGTTEGVGS P.......
98BWM018 d
         SQGTTEGVGN P.......
         PQGTTEGVGN P......
98BWMO36 a
98BWMO37_d PQGTTEGVGS P.......
99BW3932 1 SQGTTEGVGS P.......
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99BW4642 4
           SQGTTEGVGS P......
99BW4745 8
           SOGTTEGVGS P.......
99BW4754 7
           SQGTPEGVGN S..... ....
99BWMC16 8
           SQGTTEGVGS P......
           SQGAETGVGR PQTSVESSGI LGSGIEDX.
A2 CD 97CD
A2 CY 94CY
           SQGTETGVGR SQESVESSVI LGSGTEEX.
A2D___97KR
           PQGTETGVGR PQISVEPSVV LGSGTEEX.
           PQGTETGVGG .TIFVESSVI LGSRTKEQX
A2G CD 97C
           SQXTETXVXX PQISXESSXI XXSGTKEX.
A_BY_97BL0
           SQGAETGVGR HQVSVESPVI LGSGTKNX.
A KE Q23 A
A_SE SE659
           SQGVETGVGR PQVSGESPVI LGSGTKNX.
A_SE_SE725
           SOGVETGVGR POVPGEPSTV LGSGTKTX.
           SQGIETGVGR PQVSVESPVI LGSGTKEX.
A_SE_SE753
           .....VGR PQVSVESPGV LDSGTKNX.
A_SE_SE853
A SE_SE889
           SQGAETGVGG PQVSEESSII LGSGTKTX.
           ..... TQVSGESSVV LDSGTKDX.
A SE UGSE8
A_UG_92UG0
           SQGVETGVGR TQVSGESPVV LGSGTKNX.
           PQGTETGVGG PQISVESSAV LGSGTKNX.
A UG U455
           SQGVETGVGR PQVSVESPGI LGSGTKNX.
AC IN 2130
           SQGTTEGVGN PVSRKSCAVL GSGTKKEX.
AC RW 92RW
AC SE SE94
           SQGTETGVGR PQVSVESSAI LGPGTKNX.
           .....VGS NQISVESPAV LDSGTKEX.
ACD SE SE8
ACG BE VI1
           .....VGS SQTSGEHPVI LESGTKEX.
           .....VGS PQIPVEPPAV LDSGTKEX.
AD SE SE69
           .....VGS PQIPVESPAI LDSGTENX.
AD SE SE71
           .....VGD PQIPGESSAV LGTGTKEX.
ADHK NO 97
ADK_CD_MAL
           .....VGS PQISVESPAI LGSGTEEX.
           SQGTETGVGR PQIFVESSGV LGSGTKEX.
AG_BE_VI11
AG NG_92NG
           SPGTETGVGG PQISVESPVV LGSGTKEX.
           .....VGS PQISVESPTV LGTGAKEX.
AGHU GA VI
           .....VGD SQIPGESCDL LGSGTKEX.
AGU CD Z32
            .....VGD PQVSGESCPI LGEGTKEX.
AJ BW BW21
            .....VGG PQVLVESPAV LESGAAEX.
B AU VH AF
            .....VGS PQILVESPAV LDSGTKEX.
B CN RL42
            .....VGS PQILVESPAV LESGTKEX.
B DE_D31_U
           .....VGS PQVLVESPAV LEPGTKEX.
B DE HAN U
            .....VGS PQILVESPTV LESGTKEX.
B FR HXB2
B GA OYI M
           .....VGS PEILVESPAV LEPGTKEX.
B GB CAM1
            .....VGS PQILVESPAV LESGTKEX.
           .....VGS PQVLVESPAV LDPGTKEX.
B GB GB8 A
           .....VGN PQVLVESPAV LESGSKEX.
B_GB_MANC
           .....VGN PQILVESPAV LESGTKEX.
B KR WK AF
B_NL_3202A
           .....VGS PQILVESPAV LESGTKEX.
           .....VGS PQIFVESPTV LDSGTKEX.
B TW TWCYS
           .....VGS PQVLVESPTV LEPGTKEX.
B US BC LO
           .....VGT PQILVESPAV LESGTKEX.
B US DH123
            .....VGN PEILVESPTV LESGTKEX.
B US JRCSF
B_US_MNCG_
            .....VGS PQILVESPTV LESGTKEX.
B_US_P896_
            .....VGS PQILVESPAI LEPGTKEX.
            .....VGS PQVLVESPAV LESGAKEX.
B US RF_M1
B US SF2 K
            .....VGS PQILVESPAV LDSGTKEX.
B US WEAU1
            .....VGS SQILLESPAV LEPGTKEX.
            .....VGD PQILGESPTV LGSGAKEX.
B US WR27
            .....VGS PQILVESPPV LDSGTKEX.
B US YU2 M
           .....VGS PQTSGESRAV LESGTKEX.
BF1 BR 93B
C BR 92BR0
           POGNTERVGN PVFGRPCAVL ESRVKKEX.
           SQGTTEGVGN PVSGKSCAIL GSRAKKEX.
C BW 96BW0
           SQGTPEGVGN PISGKSCAVL GARAKKEX.
C BW 96BW1
C BW 96BW1
           SQGTTEGVGS PISGKSCAVL GSGTKKEX.
           SQGTTEGVGS PVSGKSCAVL GSGTKKEX.
C BW 96BW1
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C ET ETH22
           SOGTTEGVGN PISGKPCAVL GSGAKKEX.
C IN 93IN1 ....L..GS PISGKSCAVL GSGAKKEX.
C IN 93IN9
           SOGTTERVGS PISGKSCAVL GSGAKKEX.
C IN 93IN9
           SOGTTEGVGS PISGKSCAVL GYRAKKEX.
           SQGTTERVGS PISGKSCAVL GSGAKKEX.
C IN 94IN1
           SQGTTEGVGS PISGKSCTVL GSGAEKEX.
C IN 95IN2
           SQGTETGVGG PQISGESSVI LGSGTKNX.
CRF01 AE C
CRF01_AE C
           STGTETEVGR PQISGESSVI LGSGTKNX.
CRF01_AE C
           SRGTETGVGR PQISGESSVI LGSGTENX.
CRF01_AE_T
           SQGTETGVGR PQISGESSVI LGPGTKNX.
CRF01_AE T
           SQGTETGVGR PQISGESSVI LGSGTKNX.
CRF01_AE_T
           SQGTETGVGR PQISGESSVI LGPGTKNX.
CRF01_AE_T
           SQGTETGVGR PQISGESPVI LGPGTKNX.
           SQGTETGVGR PQISGESSVI LGPGTKNX.
CRF01 AE T
CRF01_AE_T
           SQGTETGVGR PQISVESSGI LGPGTKNX.
           POGTETGVGS PPISGESSTI LGSGTKEX.
CRF02_AG_F
           SQGTETGLGS PQISGESSDI LGAGTKEX.
CRF02_AG_F
           .....VAD PQIPGESRAI LGSGTKEX.
CRF02_AG_G
           SOGTETGVGS PQISVESYII LGSGTKEX.
CRF02_AG_N
CRF02_AG S
           .....VGS PQISVESSIV LGSGTKEX.
           SQGTETGVGS SQTSVESSVI LGSGTKEX.
CRF02_AG_S
           .....VGS PQILVESPTV LDSGTKEX.
CRF03_AB_R
           .....VGS PQILVESPTV LDSGTKEX.
CRF03 AB_R
CRF04_cpx_
           .....VGS PQVSVELPAV LGTGAKEX.
CRF04_cpx_
           .....VGS PQVSVEPPAV LGTGAKEX.
           .....VGN PQVPVEPPAV LGTGDKEX.
CRF04 cpx_
           .....VGS PQISVEPPAI LESGTKEX.
CRF05 DF B
CRF05_DF_B .....VGS PQISVESPTV LESGAKEX.
CRF06_cpx_ ......VGN PQISGEPDML LGTGTTEX.
CRF06_cpx_
           .....VGD PQIPGEPGVV LGTGTKEX.
           .....VGD PQIPVEPGVL LGTGTKEX.
CRF06_cpx_
           .....VGD PQIPGEPGVL LGTGTKEX.
CRF06_cpx_
           .....VGD SQISGESDTV LGPRTEEX.
CRF11_cpx_
CRF11_cpx_
            .....VGE SQIPGESSTV LGPRTEEX.
            .....VGS PQISVESPAI LESRTEEX.
D CD 84ZR0
           .....VGH PQISVESPTV LESGTEEQX
D CD ELI K
           .....VGS PQIPVEPPAV LESGTEEX.
D_CD_NDK_M
D UG 94UG1
           .....VGS HQISVESPAV LDSGTKEX.
F1 BE VI85
           .....VGS SQISGESHAV LESGTKEX.
           .....VGS SQISGESHTV LGSGTKEX.
F1_BR_93BR
           .....VGS PQISGEHHTV LESGTKEX.
F1_FI_FIN9
           .....VGN PQISMEPRTV LESGTKEX.
F1 FR MP41
F2 CM MP25
           .....VGS PQISVESRAV LGSGTKEX.
           .....LGN PQIPVEPCAV LGSGTKEX.
F2KU BE VI
G BE DRCBL
           SQGTEIGVGS PQIFVESSVV LGSGTKEX.
G NG 92NG0
           PQGTETGVGR PQVLVEPPVV LGSGTKEX.
G SE SE616
           PQGTETGVGR .SIFVESSVV LGQGTKEX.
H_BE_VI991 ......VGS PQTSGESPAV LGTGAKEX.
           .....KGG PQIPVESSTV LGTGTKEX.
H_BE_VI997
           .....EGS PQISLESSTI LGTGTKEX.
H_CF_90CF0
           .....VGD PQISGEPCMV LGAGTKEX.
J_SE_SE702
           .....VGD PQISGEPCMV LGAGTKEX.
J_SE_SE788
K_CD_EQTB1
           .....LGS PQIPVEPDTV LGSGDKEX.
           .....LGS PQISVEPCTV LESGTKEX.
K CM MP535
N CM YBF30 QQG.TATTET QNTLVGNTCI LGKRVKGX.
O_CM_ANT70 VDPR.AEDNC LQNLCSCNTI LATRIAEX.
O_CM_MVP51
           VDPG.TKDNS LT.LWSCNAI LATRIEKX.
           VDSG.TEDNC LQTLHSCNTI LATRVAEX.
O SN_MP129
O SN MP130 VDPG.TEDNC LQNLHSCNTI LATRVAEX.
U CD 83C .....VGS TQIPGESCAV LGSGTKE..
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Table 16. HIV Tat Alignment GCG Multiple Sequence File. Written by Omiga 1.1

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Name: 00BW0762_1 SEQ ID NO: 1136 Len: 108
                                              Check: 4583
                                                           Weight:
                                                                      1.00
Name: 00BW0768_2 <u>SEQ ID NO: 1137</u> Len: 108
Name: 00BW0874_2 SEQ ID NO: 1138 Len: 108
                                              Check: 5462
                                                           Weight:
                                                                      1.00
                                                           Weight:
                                                                      1.00
Name: 00BW1471_2 <u>SEQ ID NO: 1139</u> Len: 108
                                              Check: 4359
                                             Check: 5389
                                                           Weight:
                                                                      1.00
Name: 00BW1616_2 <u>SEQ ID NO: 1140</u> Len: 108
Name: 00BW1686_8 SEQ ID NO: 1141 Len: 108
                                              Check: 6742
                                                           Weight:
                                                                      1.00
Name: 00BW1759_3 <u>SEQ ID NO: 1142</u> Len: 108
                                              Check: 6187
                                                           Weight:
                                                                      1.00
                                                           Weight:
                                                                      1.00
Name: 00BW1773 2 SEQ ID NO: 1143 Len: 108
                                             Check: 5566
                                                                      1.00
                                                           Weight:
Name: 00BW1783 5 SEQ ID NO: 1144 Len: 108
                                             Check: 6579
                                                           Weight:
                                                                      1.00
Name: 00BW1795 6 SEQ ID NO: 1145 Len: 108
                                              Check: 6027
                                                           Weight:
                                                                      1.00
Name: 00BW1811 3 SEQ ID NO: 1146 Len: 108
                                              Check: 4928
Name: 00BW1859 5 SEQ ID NO: 1147 Len: 108
                                              Check: 6153
                                                           Weight:
                                                                      1.00
                                                                      1.00
Name: 00BW1880 2 SEQ ID NO: 1148 Len: 108
                                             Check: 6898
                                                           Weight:
                                              Check: 6286
                                                           Weight:
                                                                      1.00
Name: 00BW1921 1 SEQ ID NO: 1149 Len: 108
                                              Check: 4808
                                                           Weight:
                                                                      1.00
Name: 00BW2036_1 SEQ ID NO: 1150 Len: 108
                                              Check: 7492
                                                           Weight:
                                                                      1.00
Name: 00BW2063_6 SEQ ID NO: 1151 Len: 108
                                             Check: 4005
                                                           Weight:
                                                                      1.00
Name: 00BW2087 2 SEQ ID NO: 1152 Len: 108
Name: 00BW2127 2 SEQ ID NO: 1153 Len: 108
                                              Check: 6532
                                                           Weight:
                                                                      1.00
                                                           Weight:
Name: 00BW2276 7 SEQ ID NO: 1154 Len: 108
                                              Check: 7138
                                                                      1.00
Name: 00BW3819 3 SEQ ID NO: 1155 Len: 108
                                              Check: 4977
                                                           Weight:
                                                                      1.00
Name: 00BW3842_8 SEQ ID NO: 1156 Len: 108
                                             Check: 5730
                                                           Weight:
                                                                      1.00
Name: 00BW3871_3 SEQ ID NO: 1157 Len:
                                                           Weight:
                                              Check: 7576
                                                                      1.00
                                        108
Name: 00BW3876 9 SEQ ID NO: 1158 Len:
                                              Check: 4797
                                                           Weight:
                                                                      1.00
                                        108
Name: 00BW3886_8 <u>SEQ ID NO: 1159</u> Len: 108
Name: 00BW3891_6 <u>SEQ ID NO: 1160</u> Len: 108
                                              Check: 7443
                                                           Weight:
                                                                      1.00
                                              Check: 5634
                                                           Weight:
                                                                      1.00
Name: 00BW3970_2 <u>SEQ ID NO: 1161</u> Len: 108
                                              Check: 5984
                                                           Weight:
                                                                      1.00
Name: 00BW5031_1 <u>SEQ ID NO: 1162</u> Len: 108
                                              Check: 8884
                                                           Weight:
                                                                      1.00
Name: 96BW01B21 SEQ ID NO: 1163 Len: 108
                                             Check: 6237
                                                           Weight:
                                                                      1.00
Name: 96BW0407
                  SEQ ID NO: 1164 Len: 108
                                              Check: 5097
                                                           Weight:
                                                                      1.00
Name: 96BW0502
                  SEQ ID NO: 1165 Len: 108
                                              Check: 5303
                                                           Weight:
                                                                      1.00
                                                           Weight:
                                                                      1.00
Name: 96BW06_J4
                  SEQ ID NO: 1166 Len: 108
                                              Check: 5679
Name: 96BW11_06
                  SEQ ID NO: 1167 Len: 108
                                              Check: 7244
                                                           Weight:
                                                                      1.00
                  SEQ ID NO: 1168 Len: 108
                                              Check: 5043
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Name: 96BW16 26
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                                              Check: 5048
Name: 98BWMC13 4 SEQ ID NO: 1175 Len: 108
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Name: 98BWMC14 a SEQ ID NO: 1176 Len: 108
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Name: 98BWM018 d SEQ ID NO: 1178 Len: 108
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Name: 98BWMO36 a SEQ ID NO: 1179 Len: 108
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Name: 98BWM037_d SEQ ID NO: 1180 Len: 108
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Name: 99BW4642 4 SEQ ID NO: 1182 Len: 108
                                              Check: 6405
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Name: 99BW4745 8 SEQ ID NO: 1183 Len: 108
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                                              Check: 5219
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Name: 99BW4754_7 SEQ ID NO: 1184 Len: 108
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Name: 99BWMC16_8 SEQ ID NO: 1185 Len: 108
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Name: A2_CD___97 SEQ ID NO: 1186 Len: 108
                                              Check: 4523
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Name: A2_CY__
               94 SEQ ID NO: 1187 Len: 108
                                              Check: 3933
                                                           Weight:
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Name: A2D
             97_9 SEQ ID NO: 1188 Len: 108
                                              Check: 4676
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Name: A2G CD 9 SEQ ID NO: 1189 Len: 108
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                                                                      1.00
Name: A BY 97 97 SEQ ID NO: 1190 Len: 108
                                              Check: 4264
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Name: A KE 93 Q2 SEQ ID NO: 1191 Len: 108
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Name: A SE 93 SE SEQ ID NO: 1192 Len: 108
                                             Check: 4159
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Name: A SE 94 SE SEQ ID NO: 1193 Len: 108
                                             Check: 4323
                                             Check: 3099
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Name: A SE 94 SE SEQ ID NO: 1194 Len: 108
                                                           Weight:
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Name: A SE 95 SE SEQ ID NO: 1195 Len: 108
                                             Check: 3717
                                             Check: 4178
                                                           Weight:
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Name: A SE 95 SE SEQ ID NO: 1196 Len: 108
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Name: A SE 95 UG SEQ ID NO: 1197 Len: 108
                                             Check: 3954
Name: A UG 85 U4 SEQ ID NO: 1198 Len: 108
                                             Check: 3663
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Name: A UG 92 92 SEQ ID NO: 1199 Len: 108
                                             Check: 4315
                                                           Weight:
                                                                      1.00
Name: AC IN 95 2 SEQ ID NO: 1200 Len: 108
                                             Check: 5100
                                                           Weight:
                                                                      1.00
                                             Check: 4062
                                                           Weight:
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Name: AC RW 92 9 SEQ ID NO: 1201 Len: 108
Name: AC SE 96 S SEQ ID NO: 1202 Len: 108
                                             Check: 6001
                                                           Weight:
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Name: ACD_SE_95_ SEQ ID NO: 1203 Len: 108
                                             Check: 4767
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Name: ACG_BE___V SEQ ID NO: 1204 Len: 108
                                             Check: 5568
                                                           Weight:
                                                                      1.00
Name: AD SE 93 S SEQ ID NO: 1205 Len: 108
                                             Check: 4456
                                                                      1.00
                                                           Weight:
Name: AD_SE_95_S <u>SEQ_ID_NO: 1206</u> Len: 108
Name: ADHK_NO_97 <u>SEQ_ID_NO: 1207</u> Len: 108
                                             Check: 4850
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                                             Check: 6557
                                                           Weight:
                                                                      1.00
Name: ADK CD 85 SEQ ID NO: 1208 Len: 108
Name: AG BE VI SEQ ID NO: 1209 Len: 108
                                             Check: 4622
                                                           Weight:
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                                             Check: 3720
                                                           Weight:
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Name: AG_NG_92_9 SEQ ID NO: 1210 Len: 108
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                                                                      1.00
                                             Check: 4548
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                                                                      1.00
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                                             Check: 7456
Name: AGU_CD_76_ SEQ ID NO: 1212 Len: 108
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Name: AJ_BW_98_B SEQ ID NO: 1213 Len: 108
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Name: B_AU___VH_ <u>SEQ ID NO: 1214</u> Len: 108
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Name: B_DE_86_D3 SEQ ID NO: 1216 Len: 108
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Name: B DE 86 HA SEQ ID NO: 1217 Len: 108
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Name: B FR 83 HX SEQ ID NO: 1218 Len: 108
                                             Check: 2953
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Name: B GA OYI SEQ ID NO: 1219 Len: 108
                                             Check: 5056
                                                           Weight:
           CAM SEQ ID NO: 1220 Len: 108
                                                           Weight:
                                                                      1.00
Name: B GB
                                             Check: 4131
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           GB8 SEQ ID NO: 1221 Len: 108
                                             Check: 7783
                                                           Weight:
Name: B GB
                                                                      1.00
Name: B GB 59 MA SEQ ID NO: 1222 Len: 108
                                             Check: 5562
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Name: B KR WK SEQ ID NO: 1223 Len: 108
                                             Check: 6702
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Name: B_NL_86_32 SEQ ID NO: 1224 Len: 108
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                                                           Weight:
                                                                      1.00
Name: B TW
             TWC SEQ ID NO: 1225 Len: 108
                                                           Weight:
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             DH1 SEQ ID NO: 1226 Len: 108
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Name: B US
                         NO: 1227 Len: 108
                                             Check: 5087
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Name: B US
             P89 SEQ ID
                         NO: 1228 Len: 108
                                             Check: 7745
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Name: B US 83 RF SEQ ID
Name: B US 83 SF SEQ ID NO: 1229 Len: 108
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Name: B_US_84 MN SEQ ID NO: 1230 Len: 108
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Name: B US 86 JR SEQ ID NO: 1231 Len: 108
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Name: B US 86 YU SEQ ID NO: 1232 Len: 108
                                                           Weight:
                                                                      1.00
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Name: B_US_87_BC SEQ ID NO: 1233 Len: 108
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                                             Check: 5602
                                                           Weight:
Name: B_US_88_WR SEQ ID NO: 1234 Len: 108
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Name: B_US_90_WE <u>SEQ ID NO: 1235</u> Len: 108
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                                             Check: 3381
                                                           Weight:
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Name: BF1_BR_93_
Name: C_BR_92_92 SEQ ID NO: 1237 Len: 108
                                             Check: 6035
                                                           Weight:
                                                                      1.00
Name: C_BW_96_96 SEQ ID NO: 1238 Len: 108
                                             Check: 5570
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Name: C_BW_96_96 SEQ ID NO: 1239 Len: 108
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                                             Check: 5043
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                                                                      1.00
Name: C_BW_96_96 SEQ ID NO: 1240 Len: 108
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Name: C_BW_96_96 SEQ ID NO: 1241 Len: 108
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Name: C ET 86 ET SEQ ID NO: 1242 Len: 108
                                             Check: 4199
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Name: C IN 93 93 SEQ ID NO: 1243 Len: 108
                                             Check: 5957
Name: C_IN_93_93 SEQ ID NO: 1244 Len: 108
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Name: C IN 93 93 SEQ ID NO: 1245 Len: 108
                                             Check: 5361
                                                           Weight:
                                                                      1.00
                                             Check: 5479
                                                           Weight:
                                                                      1.00
Name: C IN 94 94 SEQ ID NO: 1246 Len: 108
                                             Check: 5697
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                                                                      1.00
Name: C IN 95 95 SEQ ID NO: 1247 Len: 108
                                                           Weight:
                                                                      1.00
                                             Check: 2633
Name: CRF01_AE_C SEQ ID NO: 1248 Len: 108
                                                           Weight:
                                                                      1.00
                                             Check: 4093
Name: CRF01 AE_C SEQ_ID NO: 1249 Len: 108
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Name: CRF01 AE C SEQ ID NO: 1250 Len: 108
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Name: CRF01_AE_T SEQ ID NO: 1251 Len: 108
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Name: CRF01 AE T SEQ ID NO: 1252 Len: 108
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                             1254 Len: 108
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                                                                     1.00
Name: CRF01 AE T SEQ ID NO: 1256 Len: 108
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Name: CRF02 AG F SEQ ID NO: 1257 Len: 108
                                             Check: 4840
Name: CRF02_AG_F SEQ_ID_NO:
                             1258 Len: 108
                                             Check: 6283
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Name: CRF02 AG G SEQ ID NO:
                             1259 Len: 108
                                             Check: 4683
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Name: CRF02 AG N SEQ ID NO:
                                             Check: 3989
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Name: CRF02 AG S SEQ ID NO:
                                             Check: 3401
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                                             Check: 4884
Name: CRF02 AG S SEQ ID NO: 1262 Len: 108
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Name: CRF03 AB R SEQ
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Name: CRF03 AB R SEQ ID NO: 1264 Len: 108
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Name: CRF04_cpx_ SEQ ID NO: 1265 Len: 108
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Name: CRF11_cpx_ SEQ ID_NO: 1275 Len: 108
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Name: D CD 83 ND SEQ ID NO: 1277 Len: 108
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Name: D UG 94 94 SEQ ID
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                             1279 Len: 108
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                                             Check: 4812
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                                             Check: 4376
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Name: F1 BR 93 9 SEQ ID
                         NO: 1281 Len: 108
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Name: F1 FI 93 F SEQ ID
                         NO: 1282 Len: 108
Name: F1 FR 96 M SEQ ID
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                         NO: 1283 Len: 108
Name: F2 CM 95 M SEQ
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                         NO:
                             1284 Len: 108
                                             Check: 5318
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                         NO:
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                             1289 Len:
                                             Check: 5780
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                      ID
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Name: H_CF_90_90 SEQ ID NO: 1291 Len: 108
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                         NO:
                             1292 Len: 108
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Name: J_SE_94_SE SEQ ID
                         NO:
                             1293 Len: 108
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                         NO: 1299 Len: 108
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            GRKKRSQRR. . RAPKSSPDH QNLVPKQPFS .RTNGNPTGP KEKKK.VASK
AGHU GA
            GRKKRRQRR. .GTPQDRKDH QNPVPRQPLP TTRG.NPTGP KESKKEVESK
AGU_CD_76_
           GRKKRRQRR. .TAPPGNKNH QDLVQEQPLS .QTQRKSTGP EESKKEVESK
AJ_BW_98_B
           GRKKRRQRR. .RAPEDSQTH QVSLSKQSAP QPRGD.PTGP KESKKKVESK
B_AU___VH_
           GRKKRRQRR. .RAPQDSQTH QASLSKQPAS QPRGD.PAGP KESKKKVESE
B_CN___RL4
           GRKKRRQRR. .RAPEDSQTH QVSLSKQPAS QPRGD.PTGP KESKKKVETE
B_DE_86_D3
B_DE_86_HA GRKKRRQRR. .RAPQDSQTH QVSLPKQPSS QQRGD.PDSP KKSKKKVERE
B_FR_83_HX GRKKRRQRR. .RAHQNSQTH QASLSKQPTS QPRGD.PTGP KE.KKKVERE
B_GA__OYI GRKKRRQRR. .RAPQDSKTH QVSLSKQPAS QPRGD.PTGP KESKKKVERE
       CAM GRKKRRQRR. .RTPQSSKTH QASLSKQPAS QFQGD.PTGP KESKKKVEGE
B_BB
      GB8 GRKKRRQRR. .RLPEDSQIH QVSLPKQPTS QPQGD.PTGP KESKKKVESK
B GB
B GB 59 MA GRKKRRQRR. .RAPPDSQTR QVSLSKQPTS QPRGD.PTGP EESKKKVERE
           GRKKRRQRR. .RAPQDNKNH QVSLSKQPTS RARGD.PTGQ EESKEKVEKE
B KR WK
           GRKKRRQRR. .RSPQDSETH QVSLSKQPAS QPRGD.PTGP KESKKKVERE
B NL 86 32
           GRKKRRQRR. .RTPQNSQTH QADLSKQPTS QPRGD.QTGQ KESTKKVERE
B TW
       TWC
           GRKKRRKRR. .RSPQHSQTD QASLSKQPAS QPRGD.PTGP KESKKKVETE
    DH1
B US
           GRKKRRQRR. .RPPQDSQTH QVSLSKQPSS QPRGD.PTGP KEQKKKVERE
B US P89
            GRKKRRQRR. .GPPQGSQTH QVSLSKQPTS QPRGD.PTGP KESKEKVERE
B US 83_RF
            GRKKRRQRR. .RAPQDSQTH QASLSKQPAS QSRGD.PTGP TESKKKVERE
B US 83 SF
```

```
GRKKRRORR. .RAPEDSQTH QVSLPKQPAP QFRGD.PTGP KESKKKVERE
B US 84 MN
           GRKKRRORR. .RPPQDSQTH QVSLPKQPSS QQRGD.PTGP KESKKKVERE
B US 86 JR
           GRKKRRQRR. .RPPQDSQTH QSSLSKQPTS QLRGD.PTGP TESKKKVERE
B US 86 YU
           GRKKRRQRR. .RAPQDSQTH QASLSKQPTS QPRGD.PTGP KESKKKVERE
B US 87 BC
           GRKKRRORR. . RAPPEGLTH QVPLSKQPSS QFRGD.PTGP KESKKKVVRE
B US 88 WR
           GRKKRRQRR. .RSPQNSQTH QDSLSKQPTS QPRGD.PTGP KESKKKVERE
B US 90 WE
           GRKKRRQRH. .RTPQSSQLH QDPVPKQPAS QAQGN.PTGP KESKKEVESQ
BF1 BR 93
           GRKKRRQRR. .SAPPSSEDH QNPIPKQPLP .QTRGDQTGS EESKKKVESK
C BR 92 92
C BW 96 96
           GRKKRRORR. .SAPPSSEDH QNPVSKQPLP .QTRGDPTGL EESKKKVESK
           GRKKRRQRR. .SAPPSSKDH QNPVSKQPLP .QTRGDPTGS KESKKKVESK
C BW 96 96
C BW 96 96
           GRKKRRQRR. .SAPPSSEDH QDLVPKQPLS .QARGNPTSS KESKKKVESK
C BW 96 96
           GRKKRGQRR. .SAPPRSEDH QNLISKQPLP .RTQGDSTGS EESKKKVESK
C ET 86 ET
           GRKKRRORR. .RAPOSSKOH QNLISKOPLS .HTRGDPTGS EESKKKVESK
           GRKKRRQRR. .SAPPSSEDH QNLISKQPLP .RTQGDPTGS EESKKKVESK
 IN_93_93
           GRKKRRQRR. .RAPQSSEDH QNLISKQPLP .RTQGDPTGS EESKKKVESK
 IN 93 93
           GRKKRRQRR. .SAPPSSEDH QNLISKQPLP .RTQGDPTGS EESKKKVESK
 IN_93_93
           GRKKRRQRR. .SAPQSSEDH QDLISKQPLP .RTQGDPTGS EESKKKVEGK
 _IN_94_94
           GRKKRRQRR. .SAPQSSEDH QNPISKQPLP .RTPGDPTGS EESKKKVESK
C_IN_95_95
           GRKKRKHRR. .GPPPGSKDH QNPIPKQPLP TTRG.NPTGP KESKKEVAKK
CRF01_AE_C
           GRKKRKHRR. .GPSQDSKDH QNSIPKQPLP TSRG.NPTGP KESKKKVESK
CRF01_AE_C
           GRKKRKHRR. .GTPQGSKGH QDPISKQPLP IIRG.NPTGP KESKKEVESK
CRF01_AE_C
           GRKKRKHRR. .GTPQSSKDH QNPIPKQPLP IIRR.NPTDP KESKKEVASK
CRF01_AE_T
           GRKKRKHRR. .GTPQSRKDH QHPIPEQPLS IIRG.NPTDP KESKKEVASK
CRF01 AE T
           GRKKRKHRR. .GTPQSSKDH QSPIPEQPLP IIRG.NPTDP KESKKEVASK
CRF01_AE_T
CRF01_AE_T
           GRKKRKHRR. .GTPQSRKDH QYPIPEQPLP IIRGGNPTDP KESKKEVASK
           GRKKRKHRR. .GTPQSSKDH QTPIRKQPPS IIRG.NPTDP KESKKKVESK
CRF01_AE_T
           GRKKRKHRR. .RTPQSSKDH QYPIPEQPSP IIRG.IPTDP KESKKEVASK
CRF01 AE T
           GRKKRRRRR. .GTPQSRQDH QNPVPKQPLP TTRG.DPTDP KESKKEVASK
CRF02 AG F
           GRKKRXRRR. .GTPQSRQDR QNPVSKQPLP TTRG.NPTGP KESKREVESK
CRF02 AG F
           GRKKRRRRR. .GTPQSHQDH QNPVSKQSLP QTRG.DPTGP KESKKEVESK
CRF02 AG G
           GRKKRRRR. .GTPQSRQDH QNPVPKQPLP TTRG.NPTDP KESKKEVESK
CRF02 AG N
            GRKKRKRRR. .GTPQSRQDN QDPVPKQPLP TTRG.NPAGP KESKKEVAGK
CRF02 AG S
CRF02 AG S
            GRKKRRRR. .GTPQSRQDH QNPVPKQPLP TTRG.EQTGP KESKKEVASK
           GRKKRRORR. .RAPODNOTD QVSLPKQPAS QPRGD.PTGP KE.KKKMERE
CRF03 AB R
           GRKKRRORR. .RPPQDNQTD QVSLPKQPAS QPRGD.PTGP KE.KKKVERE
CRF03 AB R
            GRKKRKHRR. .GSLQGSKGH QNLIPKQPLS QQPNGDSTGP EEQKKKVASK
CRF04_cpx_
            GRKKRKRNE. .DLLGFSRDR QNPIPKQPLS Q.PNGNPEGP KEQKKKVASK
CRF04_cpx_
            GRKKRKHRR. .RPPQGSRDR QNPIPKQPLS QQHSGDPTGP KEQKEAVASK
CRF04_cpx_
           GRKKRPRR. .RPPQGSQAH QDPVPEQPPS QPRGD.PTGP KKQKKEVESK
CRF05 DF B
CRF05 DF B
           GRKKRRSRR. .RPPQGGQAH QIPVPEQPSS QARGD.PTGQ KEQKKKVESK
            GRKKRRQRR. .QAPPGSKNH QDPVSKQPLS .QTQREQTGP EKSKKEVESK
CRF06_cpx_
            GRKKRRQRR. .TAPPGSKNH QDPVPKQPLS .QTQRGPTGP EKSKKKVESK
CRF06_cpx_
            GRKKRRQRR. .TAPPGSKNH QDPVPKQPLS .QTQRKSTGP EESKKEVESK
CRF06_cpx_
            GRKKRRQRR. .TAPLGSKSH QDPVPKQPLS .QTQRESTGP EKSKEEVESK
CRF06_cpx_
            GRKKRRQRR. .AASHSSENH QDPIPKQPST .QPNRKPTGP EESKKEVESK
CRF11_cpx_
            GRKKWRQRR. .TASRSSKNH QDPIPEQPLP .QASRNPTGP EEPKKEVESK
CRF11 cpx
            GRKKRRQRR. .GPPQGGQAH QVPIPKQPSS QPRGD.PTGP KEQKKKVESE
D CD_83_EL
D_CD_83_ND
            GRKKRRQRR. .KPPQGDQAH QVPIPEQPSS QSRGD.PTGP K.KKKKVESE
            GRKKRRQRR. .RPPHSSQTH QDPIPKQPSS QPRGD.PTGQ KEKKK.VESK
D_CD_84_84
            GRKKRRPRR. .RTPPGGQAN QDPVPKQPSS QPRGN.PTGP KEKKK.VESE
D UG 94_94
            GRKKRRQRH. .RTPQSSQVH QNSLPKQPLS QARGD.PTGP KESKKEVESK
F1_BE_93_V
            GRKKRRQRP. .RTPQSSQIH QDFVPKQPIS QARGN.PTGP KESKKEVESK
F1_BR_93_9
            GRKKRRQRH. .RTPQSSQIH QDPVPKQPLS QPRRN.PTGP KESKKEVESK
F1_FI_93_F
           GRKKRRQRR. .RTPQSSQSH KNPIPEQPLS QARGD.PTGP KESKKEVESK
F1_FR_96_M
F2_CM_95_M
           GRKKRRQRR. .RTPQSGEVH QDPVSKQPLS QTRGD.PKGP EESKKKVESK
            GRKKRRQRR. .RTPQSSQAH QNPISKQPLS QARGD.PTGP KEPKKEVESK
F2KU_BE_94
           GRKKRKHRR. .GTPHSSKDH QTPVPKQPFS TTRG.NPTGP QESKKEVESK
G_BE_96_DR
            GRKKRRPRR. .GTPQGSKDH QNPVPKQPLP ITSG.NPTGS EKPKKEVASK
G_NG_92_92
           GRKKRKHRR. .GTPQSSKGH QDPVPKQPLP TTRG.NPTGP KESKKEVASK
G_SE_93_SE
H BE___VI9
            GRKKRRORR. .GTPKSLQDH QTLIPKQPLS .RTSGDPTGP EKKKK.VASK
```

```
H BE VI9 GRKKRSRRR. .ATPASVQDH QNHIPKQPLS .RTRGDPTGP KEKKK.VASK
H_CF_90_90 GRKKRSQRH. .RTPASLQDH QNSISKQPLS .RTHGDPTGP KEQKKEVASK
J SE 93 SE GRKKRRORR. .SAPPGSKTH QDLIPKOPLS .QTQRKPTGP EESKKEVESK
J SE 94 SE GRKKRRORR. .SAPPGSKNH QDLIPEQPLF .QTQRKPTGP EESKKEVESK
K CD 97 EQ GREKRRORT. .TTPYASKNH KDPIPKQPLP .QARGDPTGP KESKKEVESK
           GRKKRRPRR. .TTPYNSENH ODPLRKOPLS .QPRGEQTDP KESKKKVESK
K CM 96 MP
N_CM_95_YB GRKKRSQRR. .RTPQSSKSH QDLIPEQPLS .QQQGDQTGQ KKQKEALESK
           GRKK...RGR PAAAS.HPDH KDPVPKQSPT ITK.RKQERQ EEQEEEVEKK
O CM ANT
O CM 91 MV GRKK...RRR PAAAASYPDN KDPVPEQSLS HTG.RKQKRQ EEQEKKVEKE
O SN 99S GRKK...RRR PAAAARHPDN QDIVPEQLTY ITN.RKQKRQ EEQEKEVENE
O SN__99S GRKK...RRR PAAAARNPDN QDIVPEQPPP ITNNRKHKRQ EEQEKEVEKE
U CD 83C GRKKRGKRR. .RTPQSGPNH QNIVSKQPSS QPRGD.PTGQ EEPKKKVEKK
            101 108
00BW0762 1
           TETDPFD.
00BW0768 2
           TKTDQFD.
00BW0874_2
           TKTDQFD.
00BW1471_2
           TEADPCD.
00BW1616_2
           TETDPFD.
00BW1686_8
           TKTDPFD.
00BW1759_3
           TETDRFD.
           TETDPD..
00BW1773_2
00BW1783_5
           TETDPFD.
00BW1795 6
           TETDPFD.
00BW1811_3
           TETDPD..
00BW1859_5
           TETDPYD.
00BW1880 2 TETNPFD.
00BW1921 1 TEADQFD.
00BW2036 1 TEADRFD.
00BW2063 6 TETDPFD.
00BW2087 2
           TERDPFD.
00BW2127 2
           TTTDPFD.
00BW2276 7
           TETDPYD.
00BW3819 3
           TKTDPFD.
00BW3842 8
           TETDRFD.
00BW3871_3
           TKTDOFD.
00BW3876 9
           TKADPFD.
00BW3886_8 AETDQFDY
00BW3891_6
           TETDPFA.
00BW3970_2
           TERDPFA.
00BW5031 1
           TETDPFDW
 96BW01B21
           TKTDPFD.
  96BW0407
           TEADPFD.
  96BW0502 TEADPFA.
 96BW06 J4
           TETDQFD.
 96BW11_06
           TETDQFD.
  96BW1210
           TETDPFD.
 96BW15B03
           TETDRFD.
 96BW16 26
           TETDPCD.
 96BW17A09 TEADPFD.
 96BWMO1_5
           TKTDQFD.
 96BWMO3_2 TETDPFD.
98BWMC12_2 TKAHPFD.
98BWMC13_4 TETDQFD.
98BWMC14_a TDTDQFA.
98BWMO14_1 TETDPCA.
98BWM018_d TETDQFD.
98BWMO36_a TETDPFD.
98BWM037_d TETDPFD.
```

99BW3932_1 TETDPFD.

```
99BW4642 4
             TETDQFA.
99BW4745_8
             TEPDPCD.
99BW4754 7
             TETDPFD.
99BWMC16 8
             TEADRFD.
A2_CD___97
             AETDRFD.
A2_CY__94
A2D__97_9
A2G_CD__9
             AETDRFD.
             AETDPCD.
             TETDPD..
A BY 97 97
             AETDQFD.
A KE 93 Q2
             AEADRFD.
A SE 93 SE
             AETDRFD.
A_SE_94_SE
             AEADRFD.
A_SE_94_SE
A_SE_95_SE
             AETDRFD.
             TEADRFD.
A_SE_95_SE
             TETDRFA.
A_SE_95_UG
             AETDRFA.
A_UG_85_U4
             AKTDRFA.
A_UG_92_92
             TEADRYA.
AC_IN_95_2
             AKTDRFD.
AC_RW_92_9
             TEADPFD.
             TETDRFD.
AC_SE_96_S
ACD SE 95
             AETDRFD.
ACG_BE____V
             TETHPLA.
AD_SE_93_S
             AEADQFDW
AD SE 95 S
             TEPDRFD.
ADHK NO 97
             TXTDPFDW
ADK_CD_85_
             AEADQFDW
AG BE VI
             TETHPGD.
AG NG 92 9
             TETDQCA.
AGHU GA
             AEADPFDW
AGU_CD 76
             TETDPFAW
AJ_BW_98_B
             AKPDRFD.
B AU VH
             TETNPSD.
B CN RL4
             TETDPRD.
B DE 86 D3
             TETDPID.
B DE 86 HA
             TEADPFD.
B FR 83 HX
             TETDPFD.
B_GA__OYI
B_GB__CAM
B_GB__GB8
             TETDPED.
             TETHPGD.
             TETDPSDW
B_GB_59_MA
             TETDPVA.
B_KR___WK_
             TVVDPVT.
B_NL_86_32
             TETDPVD.
B_TW___TWC
             TETDPNDQ
B_US__DH1
             TETDPVH.
B_US___P89
             TETDPVH.
B_US_83_RF
             TETDPAVQ
B_US_83_SF
             TETDPFD.
B_US_84_MN
             TETHPVD.
B_US_86_JR
             TETDPDN.
B_US_86_YU
             TETDPVH.
             TETDPVD.
B_US_87_BC
B_US_88_WR
             TETDPIA.
B_US_90_WE
            TETDPED.
BF1 BR 93
             AKTDPD..
C BR 92 92
             TETDPFD.
             TETDPFD.
C_BW_96_96
             TETDQFD.
C BW_96_96
             TETDPFD.
C BW 96_96
             TETDRFD.
C BW 96 96
```

```
C ET 86 ET
            AETDPYA.
C IN 93 93
            TKTDPFD.
C IN 93 93
            AKTDPFA.
C_IN_93_93
            TKTDPFA.
C_IN_94_94
            TTSDPFD.
C_IN_95_95
            TKTDPFD.
CRF01 AE C
            AKTDPFA.
CRF01_AE_C
            AETDPDW.
CRF01 AE C
            TKTDPCA.
CRF01 AE T
            AETDQCD.
CRF01_AE_T
            AETDPCD.
CRF01_AE_T
            AETDPCD.
CRF01_AE_T
            AETDPCD.
CRF01_AE_T
            AETDPD..
CRF01_AE_T
            AETDQCD.
CRF02_AG_F
            TETDQGD.
CRF02_AG_F
            TKTDPCD.
CRF02_AG_G
            TETDPFA.
CRF02_AG_N
            TKTDPCD.
CRF02_AG_S
            TETDPCD.
CRF02_AG_S
            TETGPCD.
CRF03_AB_R
            TETHPFD.
CRF03_AB_R
            TETHPFD.
CRF04_cpx_
            TEADPFA.
CRF04_cpx_
            TEADPFD.
            TESNPFD.
CRF04 cpx
CRF05_DF B
            TEADQFDW
CRF05_DF_B
            AETDPFDC
CRF06_cpx_
            AEPDRFD.
CRF06_cpx_
            AEPDRFD.
CRF06_cpx_
            AETDRFD.
CRF06_cpx_
            TEPDRFD.
CRF11_cpx_
            AEPDRFD.
CRF11_cpx_
            AEPAPFD.
D_CD_83_EL
            AETDPDC.
D_CD_83_ND
            AETDPFDW
D CD 84 84
            TEVHPFDW
D UG 94 94
            TEADPFDW
F1_BE_93_V
            AKTDPCA.
F1_BR_93_9
            AKTDPD..
F1_FI_93_F
            AKTDPCD.
F1_FR_96_M
            TETDPFD.
F2_CM_95_M
            TKTDPSD.
F2KU_BE_94
            TETDPLD.
G_BE_96_DR
            TETDPFD.
G_NG_92_92
            TETDPLD.
G_SE_93_SE
            AEADQCD.
H_BE___VI9
            TETDPFDW
H BE VI9
            TEADPCD.
H_CF_90_90
            TETDPD..
J_SE_93_SE
            AEPDRFD.
J SE 94 SE
            AEPDRFD.
K CD 97 EQ
            TKTDPD..
            TKTDQFD.
K CM 96 MP
N CM 95 YB
            TEADPCD.
O CM ANT
            AGPGGYPR
O CM 91 MV
            TGPSGQPC
O SN 99S
            ACP.RYPG
O SN 99S
            TGSDRYPR
U CD 83C
            TTTDPFD.
```

Table 17. HIV Vif Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

				_		~ 1 1			
Name:	00BW0762_1		1302		194	Check:		Weight:	1.00
Name:	00BW0768_2	SEQ ID NO:	1303	Len:	194	Check:		Weight:	1.00
Name:	00BW0874_2	SEQ ID NO:	1304	Len:	194	Check:		Weight:	1.00
Name:	00BW1471_2	SEQ ID NO:	1305	Len:	194	Check:	3843	Weight:	1.00
Name:	00BW1616_2	SEQ ID NO:	1306	Len:	194	Check:	4613	Weight:	1.00
Name:	00BW1686_8	SEQ ID NO:	1307	Len:	194	Check:		Weight:	1.00
Name:	00BW1759_3	SEQ ID NO:		Len:	194	Check:		Weight:	1.00
Name:	00BW1773_2	SEQ ID NO:	1309	Len:	194	Check:		Weight:	1.00
Name:	00BW1783_5	SEQ ID NO:	1310	Len:	194	Check:	3151	Weight:	1.00
Name:	00BW1795_6	SEQ ID NO:	1311	Len:	194	Check:	4892	Weight:	1.00
Name:	00BW1811_3	SEQ ID NO:	1312	Len:	194	Check:	3877	Weight:	1.00
Name:	00BW1859_5	SEQ ID NO:	1313	Len:	194	Check:	3290	Weight:	1.00
Name:	00BW1880_2	SEQ ID NO:	1314	Len:	194	Check:		Weight:	1.00
Name:	00BW1921_1	SEQ ID NO:	1315	Len:	194	Check:	4284	Weight:	1.00
Name:	00BW2036_1	SEQ ID NO:	1316	Len:	194	Check:	4019	Weight:	1.00
Name:	00BW2063_6	SEQ ID NO:	1317	Len:	194	Check:	4165	Weight:	1.00
Name:	00BW2087_2	SEQ ID NO:	1318	Len:	194	Check:	5068	Weight:	1.00
Name:	00BW2127_2	SEQ ID NO:	1319	Len:	194	Check:	5231	Weight:	1.00
Name:	00BW2128_3	SEQ ID NO:	1320	Len:	194	Check:	5469	Weight:	1.00
Name:	00BW2276_7	SEQ ID NO:	1321	Len:	194	Check:	5547	Weight:	1.00
Name:	00BW3819_3	SEQ ID NO:	1322	Len:	194	Check:	1251	Weight:	1.00
Name:	00BW3842_8	SEQ ID NO:	1323	Len:	194	Check:	4197	Weight:	1.00
Name:	00BW3871_3	SEQ ID NO:	1324	Len:	194	Check:	3487	Weight:	1.00
Name:	00BW3876 9	SEQ ID NO:	1325	Len:	194	Check:	4432	Weight:	1.00
Name:	00BW3886_8	SEQ ID NO:	1326	Len:	194	Check:	5175	Weight:	1.00
Name:	00BW3891 6	SEQ ID NO:	1327	Len:	194	Check:	3845	Weight:	1.00
Name:	00BW3970 2	SEQ ID NO:	1328	Len:	194	Check:	2268	Weight:	1.00
Name:	00BW5031 1	SEQ ID NO:	1329	Len:	194	Check:	3711	Weight:	1.00
Name:	96BW01B21	SEQ ID NO:	1330	Len:	194	Check:	4602	Weight:	1.00
Name:	96BW0407	SEQ ID NO:	1331	Len:	194	Check:	5108	Weight:	1.00
Name:	96BW0502	SEQ ID NO:	1332	Len:	194	Check:	4385	Weight:	1.00
Name:	96BW06 J4	SEQ ID NO:	1333	Len:	194	Check:	5371	Weight:	1.00
Name:	96BW11 06	SEQ ID NO:	1334	Len:	194	Check:	6037	Weight:	1.00
Name:	96BW1210	SEQ ID NO:	1335	Len:	194	Check:	4343	Weight:	1.00
Name:	96BW15B03	SEQ ID NO:	1336	Len:	194	Check:	5690	Weight:	1.00
Name:	96BW16 26	SEQ ID NO:	1337	Len:	194	Check:	4471	Weight:	1.00
Name:	96BW17A09	SEQ ID NO:	1338	Len:	194	Check:	3907	Weight:	1.00
Name:	96BWM01 5	SEQ ID NO:	1339	Len:	194	Check:	5608	Weight:	1.00
Name:	96BWM03 ²	SEQ ID NO:	1340	Len:	194	Check:	3079	Weight:	1.00
Name:	98BWMC12 2	SEQ ID NO:	1341	Len:	194	Check:	5336	Weight:	1.00
Name:	98BWMC13 4	SEQ ID NO:	1342	Len:	194	Check:	5304	Weight:	1.00
Name:	98BWMC14_a		1343	Len:	194	Check:	3984	Weight:	1.00
Name:	_		1344		194	Check:	2480	Weight:	1.00
Name:	98BWM018_d		1345	Len:	194	Check:	2801	Weight:	1.00
	98BWM036 a		1346		194	Check:	3762	Weight:	1.00
	98BWM037_d		1347		194	Check:	4971	Weight:	1.00
	99BW3932 1			Len:	194	Check:	4165	Weight:	1.00
Name:	99BW4642 4		1349	Len:	194	Check:	2912	Weight:	1.00
	99BW4745_8			Len:	194	Check:		Weight:	1.00
	99BW4754 7			Len:	194	Check:	3964	Weight:	1.00
Name:	. - .		1352		194	Check:	6325	Weight:	1.00
	A2 CD 97CD		1353		194	Check:	5849	Weight:	1.00
	A2_CY_94CY		1354		194	Check:		Weight:	1.00
Name:				Len:	194	Check:		Weight:	1.00
	A2G CD 97C					Check:		Weight:	1.00
	A BY 97BL0			Len:		Check:		Weight:	1.00
								-	

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Name: A KE Q23 A SEQ ID NO: 1358 Len: 194
                                             Check: 5053
                                                          Weight:
                                                                     1.00
Name: A SE SE659 SEQ ID NO: 1359 Len: 194
                                             Check: 3808
                                                          Weight:
                                                                     1.00
Name: A SE SE725 SEQ ID NO: 1360 Len: 194
                                             Check: 5856
                                                          Weight:
                                                                     1.00
Name: A SE SE753 SEQ ID NO: 1361 Len: 194
                                             Check: 5873
                                                          Weight:
                                                                     1.00
                                                                     1.00
Name: A SE SE853 SEQ ID NO: 1362 Len: 194
                                             Check: 5523
                                                          Weight:
Name: A SE SE889 SEQ ID NO: 1363 Len: 194
                                             Check: 3207
                                                          Weight:
Name: A SE UGSE8 SEQ ID NO:
                             1364 Len: 194
                                             Check: 5837
                                                          Weight:
                                                                     1.00
                             1365 Len: 194
                                             Check: 5055
                                                                     1.00
Name: A UG 92UG0 SEQ ID NO:
                                                          Weight:
1.00
                                             Check: 5386
                                                          Weight:
                                             Check: 3540
                                                                     1.00
                                                          Weight:
Name: AC RW 92RW SEQ ID NO:
                             1368 Len: 194
                                             Check: 3664
                                                          Weight:
                                                                     1.00
Name: AC SE SE94 SEQ ID NO:
                             1369 Len: 194
                                             Check: 4187
                                                          Weight:
                                                                     1.00
                             1370 Len: 194
                                                          Weight:
                                                                     1.00
Name: ACD_SE_SE8 SEQ ID NO:
                                             Check: 4653
                                                                     1.00
Name: ACG_BE_VI1 SEQ ID NO: 1371 Len: 194
                                             Check: 6680
                                                          Weight:
Name: AD_SE_SE69 SEQ ID NO: 1372 Len: 194
                                             Check: 6416
                                                          Weight:
                                                                     1.00
Name: AD_SE_SE71 SEQ ID NO: 1373 Len: 194
                                             Check: 8542
                                                          Weight:
                                                                     1.00
Name: ADHK_NO_97 <u>SEQ ID NO: 1374</u> Len: 194
                                             Check: 1255
                                                          Weight:
                                                                     1.00
Name: ADK CD MAL SEQ ID NO: 1375 Len: 194
                                             Check: 5519
                                                          Weight:
                                                                     1.00
                                                          Weight:
                                                                     1.00
Name: AG BE_VI11 SEQ ID NO: 1376 Len: 194
                                             Check: 7396
Name: AG_NG_92NG SEQ ID NO: 1377 Len: 194
                                             Check: 7120
                                                          Weight:
                                                                     1.00
Name: AGHU_GA_VI SEQ ID NO: 1378 Len: 194
                                             Check: 5827
                                                          Weight:
                                                                     1.00
                                            Check: 4744
                                                          Weight:
                                                                     1.00
Name: AGU_CD_Z32 SEQ ID NO: 1379 Len: 194
Name: AJ_BW_BW21 <u>SEQ ID NO: 1380</u> Len: 194
                                            Check: 4938
                                                          Weight:
                                                                     1.00
                                                                     1.00
Name: B AU VH_AF SEQ ID NO: 1381 Len: 194
                                             Check: 6911
                                                          Weight:
Name: B_CN_RL42_ SEQ ID NO: 1382 Len: 194
                                             Check: 6101
                                                          Weight:
                                                                     1.00
Name: B DE D31 U SEQ ID NO: 1383 Len: 194
                                             Check: 3568
                                                          Weight:
                                                                     1.00
Name: B DE HAN U SEQ ID NO: 1384 Len: 194
                                            Check: 6199
                                                          Weight:
                                                                     1.00
                                                                     1.00
Name: B_FR_HXB2_ <u>SEQ ID NO: 1385</u> Len: 194
                                             Check: 4714
                                                          Weight:
Name: B_GA_OYI__ SEQ ID NO: 1386 Len: 194
                                             Check: 4534
                                                          Weight:
                                                                     1.00
Name: B GB CAM1 SEQ ID NO: 1387 Len: 194
                                             Check: 4796
                                                          Weight:
                                                                     1.00
                                            Check: 6277
                                                          Weight:
                                                                     1.00
Name: B GB GB8 A SEQ ID NO: 1388 Len: 194
                                                          Weight:
Name: B GB MANC_ SEQ ID NO: 1389 Len: 194
                                             Check: 4800
                                                                     1.00
Name: B KR WK AF SEQ ID
                        NO: 1390 Len: 194
                                             Check: 3856
                                                          Weight:
                                                                     1.00
Name: B NL 3202A SEQ ID
                        NO: 1391 Len: 194
                                             Check: 4181
                                                          Weight:
                                                                     1.00
                                            Check: 5670
Name: B TW TWCYS SEQ ID
                         NO: 1392 Len: 194
                                                          Weight:
                                                                     1.00
                         NO: 1393 Len: 194
Name: B US BC LO SEQ ID
                                             Check: 4644
                                                          Weight:
                                                                     1.00
Name: B US DH123 SEQ ID NO: 1394 Len: 194
                                             Check: 5023
                                                          Weight:
                                                                     1.00
Name: B_US_JRCSF SEQ ID NO: 1395 Len: 194
                                             Check: 6235
                                                          Weight:
                                                                     1.00
Name: B_US_MNCG_ SEQ ID NO: 1396 Len: 194
                                            Check: 2067
                                                          Weight:
                                                                     1.00
Name: B_US_P896_ SEQ ID NO: 1397 Len: 194
Name: B_US_RF_M1 SEQ ID NO: 1398 Len: 194
                                             Check: 6322
                                                          Weight:
                                                                     1.00
                                             Check: 5045
                                                          Weight:
                                                                     1.00
Name: B_US_SF2_K SEQ ID NO: 1399 Len: 194
                                                          Weight:
                                                                     1.00
                                             Check: 3723
Name: B_US_WEAU1 SEQ ID NO: 1400 Len: 194
                                             Check: 4222
                                                          Weight:
                                                                     1.00
                 SEQ ID NO: 1401 Len: 194
                                             Check: 7503
                                                          Weight:
                                                                     1.00
Name: B_US_WR27_
Name: B_US_YU2_M SEQ ID NO: 1402 Len: 194
                                             Check: 5093
                                                          Weight:
                                                                     1.00
Name: BF1_BR_93B <u>SEQ ID NO: 1403</u> Len: 194
                                             Check: 4341
                                                          Weight:
                                                                     1.00
                                             Check: 5265
                                                          Weight:
                                                                     1.00
Name: C_BR_92BR0 <u>SEQ ID NO: 1404</u> Len: 194
                                             Check: 5846
Name: C_BW_96BW0 SEQ ID NO: 1405 Len: 194
                                                          Weight:
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                                                          Weight:
Name: C_BW_96BW1 SEQ ID NO: 1406 Len: 194
                                             Check: 3799
                                                                     1.00
                                                          Weight:
Name: C_BW_96BW1 SEQ ID NO: 1407 Len: 194
                                             Check: 4343
                                                                     1.00
Name: C_BW_96BW1 SEQ ID NO: 1408 Len: 194
                                             Check: 5690
                                                          Weight:
                                                                     1.00
Name: C_ET_ETH22 SEQ ID NO: 1409 Len: 194
                                             Check: 4205
                                                          Weight:
                                                                     1.00
Name: C_IN_93IN1 SEQ ID NO: 1410 Len: 194
                                             Check: 3033
                                                          Weight:
                                                                     1.00
Name: C_IN_93IN9 SEQ ID NO: 1411 Len: 194
                                             Check: 3201
                                                          Weight:
                                                                     1.00
                                             Check: 4905
                                                          Weight:
                                                                     1.00
Name: C IN 93IN9 SEQ ID NO: 1412 Len: 194
                                                          Weight:
                                             Check: 3129
                                                                     1.00
Name: C IN 94IN1 SEQ ID NO: 1413 Len: 194
                                             Check: 3351
                                                          Weight:
                                                                     1.00
Name: C IN 95IN2 SEQ ID NO: 1414 Len: 194
                                                          Weight:
                                                                     1.00
                                             Check: 6355
Name: CRF01 AE C SEQ ID NO: 1415 Len: 194
                                             Check: 2596
                                                          Weight:
                                                                     1.00
Name: CRF01 AE C SEQ ID NO: 1416 Len: 194
                                             Check: 4412
                                                          Weight:
                                                                     1.00
Name: CRF01 AE C SEQ ID NO: 1417 Len: 194
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Check: 5882
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                                                                     1.00
Name: CRF01 AE T SEQ ID NO: 1418 Len: 194
                                             Check: 5558
                                                          Weight:
                                                                     1.00
Name: CRF01_AE_T SEQ ID NO: 1419 Len: 194
                                                                     1.00
                                                          Weight:
Name: CRF01 AE T SEQ ID NO:
                             1420 Len: 194
                                             Check: 5926
                                                                     1.00
                                             Check: 5579
                                                          Weight:
Name: CRF01 AE T SEQ ID
                         NO:
                             1421 Len: 194
                                                                     1.00
Name: CRF01 AE T SEQ ID
                                                          Weight:
                             1422 Len: 194
                                             Check: 2960
                         NO:
Name: CRF01 AE T SEQ ID
                                                                     1.00
                                             Check: 5867
                                                          Weight:
                         NO: 1423 Len: 194
                                             Check: 1879
                                                          Weight:
                                                                     1.00
Name: CRF02 AG F SEQ ID
                         NO:
                             1424 Len: 194
                                             Check: 3893
                                                          Weight:
                                                                     1.00
Name: CRF02 AG F SEQ ID
                             1425 Len: 194
                         NO:
Name: CRF02 AG G SEQ
                                             Check: 5632
                                                          Weight:
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                      ID
                             1426 Len: 194
                         NO:
                                                                     1.00
Name: CRF02 AG N SEQ ID
                             1427 Len: 194
                                             Check: 3187
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                         NO:
Name: CRF02 AG S SEQ ID NO:
                                             Check: 5274
                                                          Weight:
                                                                     1.00
                             1428 Len: 194
                                             Check: 5177
                                                           Weight:
                                                                     1.00
Name: CRF02 AG S SEQ ID NO:
                             1429 Len: 194
                                             Check: 5215
                                                          Weight:
                                                                     1.00
Name: CRF03 AB R SEQ
                      ID NO:
                             1430 Len: 194
                                             Check: 5211
                                                                     1.00
                                                           Weight:
Name: CRF03 AB R SEQ
                             1431 Len: 194
                      ID
                         NO:
                                             Check: 2914
                                                           Weight:
                                                                     1.00
                             1432 Len: 194
Name: CRF04_cpx_ SEQ ID NO:
                                             Check: 5450
                                                           Weight:
                                                                     1.00
Name: CRF04_cpx_ <u>SEQ</u>
                      ID
                         NO:
                             1433 Len: 194
                         NO: 1434 Len: 194
Name: CRF04_cpx_ <u>SEQ</u>
                                             Check: 4358
                                                          Weight:
                                                                     1.00
                      ID
                                             Check: 7168
Name: CRF05_DF_B SEQ ID
                         NO: 1435 Len: 194
                                                           Weight:
                                                                     1.00
                                             Check: 5710
                                                           Weight:
                                                                     1.00
Name: CRF05_DF_B SEQ ID
                         NO: 1436 Len: 194
                                             Check: 4977
                                                           Weight:
                                                                     1.00
Name: CRF06_cpx_ SEQ ID
                         NO: 1437 Len: 194
Name: CRF06_cpx_ SEQ ID NO: 1438 Len: 194
                                             Check: 5603
                                                           Weight:
                                                                     1.00
Name: CRF06_cpx_ SEQ ID NO: 1439 Len: 194
                                             Check: 4458
                                                           Weight:
                                                                     1.00
                         NO: 1440 Len: 194
                                                           Weight:
                                                                     1.00
Name: CRF06_cpx_ <u>SEQ_ID</u>
                                             Check: 3711
Name: CRF11_cpx_ SEQ ID
                         NO: 1441 Len: 194
                                             Check: 4246
                                                           Weight:
                                                                     1.00
                         NO: 1442 Len: 194
Name: CRF11_cpx_ SEQ ID
                                             Check: 7186
                                                           Weight:
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                         NO: 1443 Len: 194
                                             Check: 4173
                                                           Weight:
                                                                     1.00
Name: D CD 84ZR0 SEQ ID
                         NO: 1444 Len: 194
                                             Check: 5080
                                                                     1.00
                                                           Weight:
Name: D CD ELI K SEQ ID
                                                                     1.00
                                             Check: 4285
                                                           Weight:
                         NO: 1445 Len: 194
Name: D CD NDK M SEQ ID
                         NO: 1446 Len: 194
                                                                     1.00
                                            Check: 3203
                                                           Weight:
Name: D UG 94UG1 SEQ ID
                                            Check: 5281
                                                           Weight:
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Name: F1 BE VI85 SEQ ID
                         NO:
                             1447 Len: 194
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Name: F1 BR 93BR SEO ID
                             1448 Len: 194
                                            Check: 2780
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                         NO:
Name: F1 FI FIN9 SEQ ID
                             1449 Len: 194
                                            Check: 3522
                                                           Weight:
                                                                     1.00
                         NO:
Name: F1 FR MP41 SEQ ID
                         NO: 1450 Len: 194
                                            Check: 3777
                                                           Weight:
                                                                     1.00
                                            Check: 5402
                                                           Weight:
                                                                     1.00
Name: F2 CM MP25 SEQ ID
                         NO:
                             1451 Len: 194
                                                           Weight:
                                                                     1.00
Name: F2KU BE VI SEQ ID
                         NO:
                             1452 Len: 194
                                            Check: 6170
                                                           Weight:
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Name: G BE DRCBL SEQ ID
                         NO:
                             1453 Len: 194
                                            Check: 6155
Name: G_NG_92NG0 SEQ ID NO:
                             1454 Len: 194
                                             Check: 5616
                                                           Weight:
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Name: G SE SE616 SEQ ID
                             1455 Len: 194
                                             Check: 6641
                                                           Weight:
                                                                     1.00
                         NO:
Name: H BE VI991 SEQ
                      ID
                         NO:
                             1456 Len: 194
                                             Check: 5850
                                                           Weight:
                                                                     1.00
Name: H BE_VI997 SEQ ID
                                                           Weight:
                                                                     1.00
                         NO: 1457 Len: 194
                                             Check: 6598
Name: H CF 90CF0 SEQ ID
                         NO: 1458 Len: 194
                                             Check: 4443
                                                           Weight:
                                                                     1.00
                                             Check: 6028
                                                           Weight:
                                                                     1.00
Name: J SE SE702 SEQ ID
                         NO: 1459 Len: 194
Name: J SE SE788 SEQ ID NO: 1460 Len: 194
                                             Check: 5724
                                                           Weight:
                                                                     1.00
Name: K CD EQTB1 SEQ ID NO: 1461 Len: 194
                                                                     1.00
                                             Check: 6926
                                                           Weight:
Name: K_CM_MP535 SEQ ID
                         NO:
                             1462 Len: 194
                                             Check: 6479
                                                           Weight:
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Name: N_CM_YBF30 SEQ ID NO:
                                                                     1.00
                             1463 Len: 194
                                             Check: 4619
                                                           Weight:
Name: O_CM_ANT70 SEQ ID
                         NO:
                             1464 Len: 194
                                             Check: 412
                                                           Weight:
                                                                     1.00
Name: O_CM_MVP51 SEQ ID NO:
                             1465 Len: 194
                                             Check: 6622
                                                           Weight:
                                                                     1.00
Name: O_SN_99SE_ <u>SEQ ID NO: 1466</u> Len: 194
                                             Check: 8844
                                                           Weight:
                                                                     1.00
Name: O_SN_99SE_ <u>SEQ ID NO: 1467</u> Len: 194
                                             Check: 9492
                                                           Weight:
                                                                      1.00
Name: U_CD___83C SEQ ID NO: 1468 Len: 194
                                             Check: 5631
                                                           Weight:
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SEQ ID NO
                       MENRWQVLIV WQVDRMKIRT WNSLVKHHMY VSKRANGWFY RHHYESRHPK
           00BW0762_1
1302
                        MENRWQGLIV WQVDRMKIRT WNSLVKHHMY VSRRANGWFY RHHYESRHPK
           00BW0768_2
1303
                       MENRWQVLIV WQVDRMKIRA WNSLVKHHMY ISRKASGWFY RHHYESRHPK
           00BW0874 2
1304
1305
           00BW1471 2
                       MENRWQVLIV WQVDRMKIRT WNSLVKHHMY ISRRAKGWVY RHHYESRHPR
                       MENRWQVLIV WQVDRMRIRT WNSLVKHHMY VSRRASGWFY RHHYESRHPK
           00BW1616 2
1306
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1307	00BW1686_8	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	ISRRASGWSY	RHHYESRHPK
<u>1308</u>	0BW1759_3	MENRWQVLIV	WQVDRMKIRT	${\tt WNSLVKHHMY}$	ISKRAKGWLY	RHHYENRHPK
<u>1309</u>	00BW1773_2	MENRWQVLIV	WQVDRMKIKT	${\tt WNSLVKHHMY}$	VSKRAKGWFY	RHHYESSHPR
<u>1310</u>	00BW1783_5	MENRWQVLIV	WQVDRMRIRT	WNSLVKHHMY	ISKKARGWFY	RHHYESRHPK
<u>1311</u>	00BW1795_6	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	VSRKANGWFY	RHHYESRHPK
1312	00BW1811_3	MENRWQVLIV	WQVDRMKIKT	WNSLVKHHMY	ISKKAKGWFY	RHHYESRNPK
<u>1313</u>	00BW1859_5	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	ISRKAKGWYY	RHHFESRHPK
1314	00BW1880_2	MENRWQVLIV	WQIDRMKIRT	WNSLVKHHMY	ISRRASGWFY	RHHYESRNPK
1315	00BW1921_1	MENRWQVLIV	WQIDRMKIRT	WNSLVKHHMY	ISRRANGWFY	RHHYESRHPK
1316	00BW2036_1	MENRWQALIV	WQVDRMRIRT	WNSLVKHHMH	VSKRAKGWFY	RHHFESRHPK
1317	00BW2063_6	MENRWQGLIV	WQVDRMRIRT	WNSLVKHHMY	ISRRASGWFY	RHHYDSRHPK
1318	00BW2087_2	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	ISRRAAGWFY	RHHYESRNPR
1319	00BW2127_2	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	TSKKATGWFY	RHHYESRHPK
<u>1320</u>	00BW2128_3	MENRWQVLIV	WQVDRMRIRT	WNSIVKHHMY	VSRRTNGWFY	KHHYESRNPK
<u>1321</u>	00BW2276_7	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	ISRRTMGWFY	RHHFQSRHPK
1322	00BW3819_3	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMH	ISKRAKGWFY	RHHFESRHPK
1323	00BW3842_8	MENRWQALIV	WQVDRMRIRT	WNSLVKHHMY	ISRRASGWFY	RHHFESRHPK
1324	00BW3871_3	MENRWQVLIV	WQVDRMRIRT	WNSLVKHHMY	ISRRASGWFY	RHHYESRHPK
1325	00BW3876_9	MENRWQVLIV	WQVDRMRIRT	WNSLVKHHMY	VSRKAHGWFY	RHHYQSRHPK
<u>1326</u>	00BW3886_8	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	ISKRANGWFY	RHHYQSRHPK
<u>1327</u>	00BW3891_6	MENRWQVMIV	WQVDRMKIRT	WNSLVKHHMY	VSKKANGWFY	RHHYESRHPR
1328	00BW3970_2	MENRWQVLIV	WQIDRMRIKT	WNSLVKHHMY	VSRRASGWFY	RHHFESRHPK
1329	00BW5031_1	MDNRWQGLIV	WQVDRMRIRT	WNSLVKHHMY	VSRRANGWFY	RHHHESRHPK
1330	96BW01B21	MENRWQVLIV	WQVDRMRIRT	WNSLVKHHMY	VSRRASGWFY	RHHFESRHPK
1331	96BW0407	MENRWQVMIV	WQVDRMKIRT	WNSLVKHHMY	VSKKAKGWFY	RHHYESRHPR
1332	96BW0502	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMH	ISKRAKGWFY	RHHYESRHPK
<u>1333</u>	96BW06_J4	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	ISKRANGWFY	RHHYESRHPK
1334	96BW11_06	MENRWQALIV	WQVDRMRIRT	${\tt WTSLVKHHMY}$	VSRRANGWYY	RHHYESRHPK
<u>1335</u>	96BW1210	MENRWQGLIV	WQVDRMRIRT	${\tt WHSLIKHHMY}$	VSKRADGWFY	RHHYESRHPK
1336	96BW15B03	MENRWQALIV	WQVDRMRIRT	WNSLVKHHMY	VSKRTNGWFY	RHHFESRHPK
1337	96BW16_26	MENRWQVLIV	WQVDRMKIKT	${\tt WNSLVKHHMY}$	ISRRANGWSY	${\tt GHHYESRNPK}$
1338	96BW17A09	MENRWQVLIV	WQVDRMKIRT	${\tt WNSLVKHHMY}$	ISRRAKGWFY	RHHYESRHPK
1339	96BWMO1_5	MENRWQGLIV	WQVDRMKIRT	${\tt WNSLVKHHMY}$	VSKRAAGWWY	RHHYESRHPK
<u>1340</u>	96BWMO3_2	MENRWQVLIV	WQVDRMRIRT	${\tt WNSLVKHHMY}$	VSKKAAGWFY	RHHYESRHPK
<u>1341</u>	98BWMC12_2	MENRWQVLIV	WQVDRMRIRT	${\tt WNSLVKHHMY}$	TSGRASGWFY	RHHYESRHPK
1342	98BWMC13_4	MENRWQVLIV	WQVDRMKIRT	${\tt WNSLVKHHMY}$	VSKRAKGWYY	RHHYESRHPK
1343	98BWMC14_a	MENRWQGLIV	WQVDRMKIRT	WNSLVKHHMY	ISRRASGWFY	RHHFESRHPK
1344	98BWM014_1	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	ISRRAKGWIY	KHHFESRNPK
<u>1345</u>	98BWM018_d	MENRWQVLIV	WQVDRMRIRT	WNSLVKHHMY	VSKRAKGWFY	RHHYESRHPK
<u>1346</u>	98BWMO36_a	MENRWQVLIV	WQVDRMRIRA	WNSLVKHHMH	ISKRAAGWFY	RHHYESRNPK
1347	98BWM037_d	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	VSKRASKWFY	RHHYESRHPK
1348	99BW3932_1	MENRWQVLIV	WQVDRMRIRT	WNSLVKHHMY	ISRRAEGWFY	RHHYESRHPK
1349	99BW4642_4	MENRWQVLIV	WQIDRMKIRT	WNSLVKHHMY	VSKRAKGWFY	RHHFESRHPK
1350	99BW4745_8	MENRWQVLIV	WQVDRMRIRT	WNSLVKHHMH	ISRRANGWFY	RHHYESRHPR
1351	99BW4754_7					RHHYESRHPK
<u>1352</u>	99BWMC16_8	MENRWQGLIV	WQVDRMRIRT	WNSLVKHHMH	VSRRANGWFY	RHHYESRHPK
<u>1353</u>	A2_CD_97CD	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	VSKKAREWFY	RHHYESRHPR

1354	A2_CY_94CY		WQVDRMRIRT			
1355	A2D97KR		WQVDRMRIRT			
1356	A2G_CD_97C		WQVDRMRIKR			
<u>1357</u>	A_BY_97BL0		WQVDRMRIRT			
1358	A_KE_Q23_A	MENRWQAMIV	WQVDRMRIRT	WNSLVKHHMH	VSKKAKRWFY	RHHYESRHPK
<u>1359</u>	A_SE_SE659	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	VSKKAKNWVY	RHHFESRHPK
<u>1360</u>	A_SE_SE725	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	VSRKAKDWFY	RHHYESRNPR
1361	A_SE_SE753	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMC	VSKKARNWFY	RHHYESRHPK
1362	A_SE_SE853	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	ISKKAKNWFY	RHHFESRHPK
<u>1363</u>	A_SE_SE889	MENRWQVMVV	WQVDRMRIRT	WNSLVKHHMY	ISKKAKGWLY	RHHFESRHPK
<u>1364</u>	A_SE_UGSE8	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	ISKKAAGWFY	RHHYESRHPK
<u>1365</u>	A_UG_92UG0	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	ISRRAKGWFY	RHHYESRHPK
<u>1366</u>	A_UG_U455_	MENRWQVMIV	WQVDRMKIRT	WNSLVKHHMY	VSKKAQGWFY	RHHYESRHSR
<u>1367</u>	AC_IN_2130	MENRWQALIV	WQVDRMKIRT	WNSLVKHHMY	VSRKANGWFY	RHHYDSRHPK
1368	AC_RW_92RW	MENRWQVMIV	WQVDRMKIRT	WNSLVKHHMY	ASRRAKGWFY	RHHYESRHPK
1369	AC_SE_SE94	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	ISKKAKRWFY	RHHYESRHPK
1370	ACD_SE_SE8	MENRWQVMIV	WQVDRMRIGT	N.SLVKHHMY	VSKKARGWFY	RHHYXTRHPR
1371	ACG_BE_VI1	MENRWQVMVV	WQVDRMRIRT	WHSLVKHHMY	TSKKAKNWCY	RHHYESMHPK
1372	AD_SE_SE69	MENRWQVMIV	WQVDRMRIRT	WKSLVKYHMY	VSKQARGWLY	RHHYDCLNPK
1373	AD_SE_SE71	MENRWQVMIV	WQVDRMRIKT	WNSLVKHHMY	VSKKAQNWVY	RHHYESRHPR
1374	ADHK_NO_97	MENRWQVMIV	WQVDRMRIRT	WHSLVKHHIY	VSKKANKWLF	RHHYESRHPK
1375	ADK_CD_MAL	MENRWQVMIV	WQVDRMRIRT	WHSLVKHHMY	VSKKAKNWFY	RHHYESRHPK
1376	AG_BE_VI11	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	VSKKAKGWFY	RHHYESRHPK
1377	AG_NG_92NG	MENRWQVVIV	WQVDRMRIRT	WNSLVKYHMY	KSKKAKDWFY	RHHYESRHPK
1378	AGHU_GA_VI	MENRWQVMIV	WQVDRMRIST	WKSLVKHHMY	VSKKAQGWFY	RHHYDCTHPR
1379	AGU_CD_Z32	MENRWQVMIV	WQVDRMRINT	WKGLVKYHMY	KSKKAKNWFY	RHHYDSNHPK
1380	AJ_BW_BW21	MENRWQVMIV	WQVDRMRINT	WKSLVKYHMH	VSKKTKKWLY	RHHYDSNHPK
1381	B_AU_VH_AF	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHLY	KSGKARRWVY	RHHYESTHPR
1382	B_CN_RL42_	MENRWQVMIV	WQVDRMRIKT	WKSLVKHHMY	ISRKAKGWFY	KHHYDSTHPK
1383	B_DE_D31_U	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	VSGKAEKWFY	KHHYESTNPR
1384	B_DE_HAN_U	MENRWAVMIV	WQVDRMRIRT	WNSLVKHHIY	CSRKAKNWVY	RHHYESTNPR
1385	B_FR_HXB2_	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	VSGKARGWFY	RHHYESPHPR
1386	B_GA_OYI	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	VSKKAKGWFY	RHHYESTHPR
1387	B_GB_CAM1_	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	ISGKAKKWSY	RHHYESTHPR
1388	B_GB_GB8_A	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	ISGKAKKWVY	KHHYENTHPR
1389	B_GB_MANC_	MESRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	ISGKAKRWSY	KHHYESTNPR
1390	B_KR_WK_AF	MENRWQVMIV	WQVDRMRIKT	WKSLVKHHMY	ISKKAKEWVY	RHHYESTHPR
1391	B_NL_3202A	MENRWQVMIV	WQVDRMRIRA	WKSLVKHHMY	KSKKAERWFY	RHHYESTHPR
1392	B_TW_TWCYS	MENRWQVMIV	WQVDRMRIRA	WKSLVKHHMY	ISKKAKGWLY	KHHYESTHPR
1393	B_US_BC_L0	MENRWQVMIV	WQVDRMRIRT	WISLVKHHMY	ISRKAKGWFY	RHHYESTHPK
1394	B_US_DH123	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	VSKKAKGWFY	RHHYESTHPR
1395	B_US_JRCSF	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	ISGKAKGWIY	KHHYESTNPR
1396	B_US_MNCG_	MENRRQVMIV	WQADRMRIRT	WKSLVKHHMY	ISKKAKGRFY	RHHYESTHPR
1397	B_US_P896_	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	ISGKAKGWSY	RHHYESTNPR
1398	B_US_RF_M1	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	ISRKAKGWFY	RHHYESTHPR
1399	B_US_SF2_K	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	ISKKAKGWFY	RHHYESTHPR
1400	B_US_WEAU1	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	ISKKAKGWSY	RHHYESTHPR

<u>1401</u>	B_US_WR27_	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHXH	ISGKARRWXY	XHHYENNHPR
1402	B_US_YU2_M	MENRWQVMIV	WQVDRMRIRA	WKSLVKHHMY	ISGKARGWFY	RHHYESPHPR
1403	BF1_BR_93B		-	WKSLVKYHMH		
1404	C_BR_92BR0	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	VSRRASGWYY	RHHYESRHPK
1405	C_BW_96BW0	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	VSRKANGWFY	RHHYESRHPR
1406	C_BW_96BW1	MENRWQVLIV	WQVDRMRIRT	WTSLVKHHMY	VSRRANGWSY	RHHFESRHPK
1407	C_BW_96BW1	MENRWQGLIV	WQVDRMRIRT	WHSLIKHHMY	VSKRADGWFY	RHHYESRHPK
1408	C_BW_96BW1	MENRWQALIV	WQVDRMRIRT	WNSLVKHHMY	VSKRTNGWFY	RHHFESRHPK
1409	C_ET_ETH22	MENRWQVLIV	${\tt WQVDRMKIRT}$	WNSLVKHHMH	ISRRANGWVY	RHHYDSRHPK
1410	C_IN_93IN1	MENRWQVLIV	${\tt WQVDRMKIRT}$	WNSLVKHHMY	VSRRAKGWFY	RHHYDSRHPK
1411	C_IN_93IN9	MENRWQVLIV	WQVDRMKIRT	${\tt WNSLVKHHMY}$	VSRRANGWFY	RHHYESRHPK
1412	C_IN_93IN9	MENRWQVLIV	${\tt WQVDRMKIRT}$	WNSLVKHHMY	VSRRATGWFY	RHHYESRNPK
1413	C_IN_94IN1	MENRWQVLIV	WQVDRMKIRT	${\tt WNSLVKHHMY}$	VSRRANGWFY	RHHYDSRNPK
1414	C_IN_95IN2	MENRWQVLIV	WQVDRMKIRT	WNSLVKHHMY	VSRRANGWFY	RHHYESRHPK
1415	CRF01_AE_C	MENRWQVMIV	WQVDRMRIRT	${\tt WYSLVKHHMY}$	ISKKAKNWFY	RHHYESQHPK
1416	CRF01_AE_C	MENRWQVMIV	WQVDRMRIRA	${\tt WNSLVKHHMY}$	SSKKAAKWFY	RHHYESQHPK
1417	CRF01_AE_C	MENRWQVMIV	WQVDRMRIKT	WNSLVKHHMY	ISKKAKKWVY	RHHYESQHPK
1418	CRF01_AE_T	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHMY	ISKKAKKWFY	RHHYESQHPK
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1423	CRF01_AE_T	MENRWQVMIV	WRVDRMRIRT	WNSLVKHHMY	ISKKAKNWFY	RHHYESQHPK
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1430	CRF03_AB_R	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHIY	ISKKARGWVY	KHHYESRNPR
1431	CRF03 AB R	MENRWQVMIV	WQVDRMRIRT	WNSLVKHHIY	ISKKARGWVY	KHHYESRNPR
1432	CRF04_cpx_	MANRWQVMIV	WQVDRMKIRT	WNSLVKHHMY	VSKKAKGF.Y	RHHYESRHPK
1433	CRF04_cpx_	MENRWQVMIV	WQVDRMKIRT	WNSLVKHHMY	ISKKAKGWSY	RHHYESRHPR
1434	CRF04_cpx_	MENRWQVMTV	WQVDRMKIRT	WNSLVKHHMH	ISKKAKGWVY	KHHYESRNPR
1435	CRF05_DF_B	MENRWQVMIV	WQVDRMRINT	WKSLVKYHMH	VSKKANRWCY	RHHFESRNPR
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1437	CRF06_cpx_	MENRWQVMIV	WQVDRMRINT	WKSLVKYHMH	ISKKAKRWNY	RHHYDSNHPK
1438	CRF06_cpx_	MENRWQVMIV	WQVDRMRINT	WKSLVKYHMH	ISKKAKRWTY	RHHYDSNHPK
1439	CRF06_cpx_	MENRWQVMIV	WQVDRMRINA	WKSLVKYHMN	VSKKAKGWLY	RHHYDSNHPK
1440	CRF06_cpx_	MENRWQVMIV	WQVDRMRINT	WKSLVKYHMH	ISKKARKWAY	RHHYDSHHPK
1441	CRF11 cpx_	MENRWQVMIV	WQVDRMRIRT	WHSLVKHHMY	VSKKARRWMY	RHHYESRHPK
1442	CRF11_cpx_	MENRWQVMIV	WQVARMRIRT	WNSLVKHHMY	VSKKAKGWLY	RHHYESRHPR
1443	D_CD_84ZR0	MENRWQVMIV	WQVDRMRINT	WKSLVKYHMH	ISKKAKGWFY	RHHYDSPHPK
1444	D_CD_ELI_K	MENRWQVMIV	WQVDRMRIKT	WKSLVKHHMY	VSKKANRWFY	RHHYESPHPK
1445	D_CD_NDK_M	MENRWQVMIV	WQVDRMRINT	WKSLVKYHMY	VSKKANRWFY	RHHYDSHHPK
1446	D_UG_94UG1	MENRWQVMIV	WQVDRMRIRT	WKSLVKHHMY	ISKKAKGWLY	RHHYDCPNPK
1447	F1_BE_VI85	MENRWQLMIV	WQVDRMRINT	WKSLVKYHMY	VSKKAKGWSY	RHHFQSRHPR

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                       MENRWQVTIV WQVDRMRINT WKSLVKYHMH VSKKAKRWFY RHHFESRHPK
1449
           F1 FI FIN9
           F1 FR MP41 MENRWQVMIV WQVDRMRIST WKSLVKYHMH VSKKAKNWFY RHHFQSRHPK
1450
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B GB MANC
B KR WK AF ISSEVHIPLG D.AKLVITTY WGLHTGEREW HLGQGVSIEW RKKRYNTQVD
B NL 3202A ISSEVHIPVG E.ARLVITTY WGLHTGERDW HLGQGVSIEW RKKRYSTQVD
B_TW_TWCYS ISSEVHIPLG D.ATLVITTY WGLHTGERDW HLGQGVSIEW RKRRYSTQVD
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B US_JRCSF VSSEVQIPLG D.ARLVITTY WGLHTGERDW HLGQGVSMEW RTRRYSTQVD
B US MNCG
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B_US_RF_M1 ISSEVHIPPG D.ERLVITTY WGLHTGERDW HLGQGVSIEW RKRRYSTQVD
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B US WEAU1 ISSEVHIPLG E.GKLVITTY WGLHTGERDW HLGQGVSIEW RKQRYSTQVD
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BF1_BR_93B
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C_IN_95IN2 VSSEVHIPLG E.ARLVITTY WGLQTGERDW HLGHGVSIEW RLRKYSTQVE
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G SE SE616 VSSEVHIPLG D.ATLVVTTY WGLHTGEKDW QLGHGVSIEW RQRRYRTQVE
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BF1 BR 93B LTALIKPKKR KPPLPSVKKL TEDRWNKPQK TKDHRGSHTM NGH.
C_BR_92BR0 LTALIKPKKI KPPLPSVKKL VEDRWNKPQK TRDRRGNHTM NGH.
C BW 96BWO LTALIKPKKR KPPLPSVRKL VEDRWNEPQK TRGRRGNHTM NGH.
C BW 96BW1 LTALIKPKKI KPPLPSVRKL VEDRWNKPQK TRGRRGNHTM NGH.
C BW 96BW1 LTALIKPKKR KPPLPSVRKL VEDRWNKPQK TRGRKGNHTM NGH.
           LTALIKPKQI KPPLPSVRKL VEDRRNKPQK TRGRRGNRTM NGH.
C BW 96BW1
           LTALIKPKKA KPPLPSVSKL VEDKWNKPQK TRGRRGNHTM NGH.
C ET ETH22
C IN 93IN1 LTALIKPKKI KPPLPSIKKL VEDRWNNPQK IRGRRGNHTM NGH.
           LTALIKPKKI KPPLPSIKKL VEDRWNNPQK IRGRRGNHTM NGH.
C IN 93IN9
           LTALIKPKKI KPPLPSVRKL VEDRWNNPLK TRGRRGNHTM NGH.
C IN 93IN9
           LTALIKPKKI KPPLPSIKKL VEDRWNNPQK IRGRRGNHTM NGH.
C IN 94IN1
           LTALIKPKKI KPPLPSIKKL VEDRWNNPQK IRGRKGNHIM HGH.
C_IN_95IN2
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LKALATPKKT RPPLPSVRKL TEDRWNKPQK TRGHRENPTM NGH.
CRF01 AE C
           LKALTKTKKT KPPLPSVRKL TEDRWNKPQK TKGHRESPTM NGH.
CRF01 AE C
           LKALATPKKI RPPLPSVRKL TEDRWNKPQK TRGHRENPTM SGH.
CRF01 AE C
CRF01_AE_T
           LKALTTPKRI RPPLPSVKKL TEDRWNKPQK IWGHRENPTM NGH.
           LKALTTPKRI KPPLPSVKKL TEDRWNKPQK IRDHREYRTM NGH.
CRF01 AE T
           LKALTTPKRI RPPLPSVKKL TEDRWNKPQK IKGHRENPTM NGH.
CRF01 AE T
CRF01 AE T LKALTTPKRI RPPLPSVKKL TEDRWNKHQ. KGDHRENPTM NGH.
CRF01 AE T LKALTTPKRI RPPLPSV.EI TEDRWNKPQ. KRGHRENPTM NGH.
CRF01_AE_T LKALTTPKRI KPPLPSVRKL TEDRWNEPQK IRGHREYPTM NGH.
CRF02 AG F LKALVTPAKT KPPLPSVKKL AEDRWNKPQK TRGHRGNRSM NGH.
CRF02 AG F LKALVTPVKT KPPLPSVKKL AEDRWNKPQK TRGHRGNRSM NGQ.
CRF02_AG_G LKALVTPTRK KPPLPSVRKL AEDRWNEPQK TRGHRGSRPM NGR.
CRF02 AG N LNALVAPTKT KPPLPSVRKL AEDRWKEPQK TRGHRGSRPM NGH.
CRF02_AG_S LKALVTPTRT KPPLPSVKKL AEDRWNEPQK TRGHRGSRSM NGH.
CRF02_AG_S LKALVTPTRR KPPLPSVKKL AEDRWNEPQK TRGHRGNRSM NGH.
CRF03_AB_R LAALRTPKKI KPPLPSVTKL TEDRWNKPQR TKDHRGSHTM SGH.
CRF03_AB_R LAALRTPKKI KPPLPSVTKL TEDRWNKPQR TKDHRGSHTM SGH.
CRF04_cpx_ LAALISPKKT KPPLPSVKKL VEDRWNKPQK TRGRRENQIM NGH.
CRF04_cpx_ LAALISPKKT KPPLPSVKKL VEDRWNKPQK TRGRRENQIM NGH.
CRF04_cpx_ LAALISPKKT KPPLPSVKKL VEDRWNKSQK TKGRRESHIM NGH.
CRF05 DF B LTALITPKKT KPPLPSVRKL TEDRWNKPQK TKGRRGNHTM NGY.
CRF05 DF B LTALITPQKI KPPLPSVRKL TEDRWNKPQR TKGHRGCHTM NGY.
CRF06_cpx_
           LTALIKPEKR KPPLPSVQKL VEDRWNKPQK TRGHRESHTM NGH.
CRF06_cpx_
           LTALIKPKKR KPPLPSVQKL VEDRWNKPQK TRDHRESHTM NGH.
           LTALIKPRKR KPPLPSVQKL VEDRWNKPQK TRDHRECHTM NGH.
CRF06_cpx_
CRF06_cpx_
           LKALVKTKRR KPPLPSVQKL VEDRWNKPQK TKDHRESHIM DGH.
           LKALVTPTRA KPPLPSVRKL AEDRWNKPQK TRGHRGNHTA NGC.
CRF11_cpx_
CRF11_cpx_
           LKALVTPKRT KPPLPSVRKL TEDRWNKPQK TRGRRGNHTV NGC.
           LTALIAPKKR KPPLPSVKKL TEDRWNKPRQ TKGRRGSHTM NGH.
D CD 84ZR0
D CD ELI K LTALIAPKQI KPPLPSVRKL TEDRWNKPQQ TRGHRGSHTM NGH.
D CD NDK M LAALIAPKKI KPPLPSVRKL TEDRWNKPQK TKGRRGSHTM NGH.
           LTALVTPRKI KPPLPSVGKL TEDRWNKPQR TKGHRGSHTM NGH.
D UG 94UG1
           LTALIAPEKT KPPLPSVQKL VEDRWNKPQE TRGHRGSHTM NGH.
F1 BE VI85
           LTALIAPKKT KPPLPSVQKL VEDRWNKPQK TRGHRESHTM NGH.
F1 BR 93BR
           LTALVSPKKA KPPLPSVKKL VEDRWNKPQE IRGHRGSHTM NGH.
F1 FI FIN9
           LTALIAPKKT KPPLPSVKKL VEDRWNKPQE TRGHRGSHTM NGH.
F1 FR MP41
           LTALITPKKI KPPLPSVRKL VEDRWNNPQK TRGHRGSHTM NGH.
F2 CM MP25
F2KU BE VI LTALVAPKKT KPPLLSVRKL VEDRWNKPQK TRDHRGSHTM NGH.
G BE DRCBL LKVLVAPTRR RPPLPSVRKL TEDRWNEPQK TRGHRENPTM NGH.
G NG 92NG0 SKALVTPTRK RPPLPSVGKL AEDRWNKPQK TRDHRENPTM NGH.
G_SE_SE616 LKVLVTSKRS RPPLPSVTEL AEDRWNKPQK TRGHRENPTM NGH.
H_BE_V1991 LTALISPKRT KPPLPSVRKL VEDRWNKPQK TRGHRGSHTM NGH.
H_BE_V1997 LTALVAPKKT KPPLPSVKKL VEDGWNKPQK TRGHRGSHTM NRH.
H_CF_90CF0 LTALVAPKKI KPPLPSVRKL VEDRWNKPQK TRGHRGSHTM NGH.
J_SE_SE702 LTALIKPKRR KPPLPSVQKL VEDRWNKPQK TRDHRESHTM NGH.
J_SE_SE788 LTALIRPKRR KPPLPSVQKL VEDRWNKPQK TTGHRESHTM NGH.
K_CD_EQTB1 LTALIAPKKT KPPVPSVQKL VEDRWNKPQK TRGHRGSHTM SGQ.
K_CM_MP535 LTALVAPRRP KPPVPSVKKL VEDRWNKPQK TRGHRGSQTM NGH.
N_CM_YBF30 LTAWVGAKKR KPPLPSVTKL TEDRWNEHQK MQGHRGNPIM NGH.
O CM ANT70 LRAVVKARSR KPPLPSVQKL TEDRWNKHLR IRDQLKSPSM NGH.
O CM MVP51 LKAVVKVKRN KPPLPSVQRL TEDRWNKPWK IRDQLGSHSM NGH.
            LRVVVKEKRN KPPLPSVQKL TEDRWSRHLR IRDQLESHSM NGH.
O_SN_99SE_
            LRVVVKEKRH KPPLPSVQKL TEDRWSRHLR IRDQLGSHSM NGH.
O SN 99SE
U CD 83C LTTLVAPTKR KPPLPSVRKL VEDRWNKPQK TKGHKGSHTM HGH.
```

Table 18. HIV Vpr Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

Name:	00BW0762_1		1469		100	Check:		Weight:	1.00
Name:	00BW0768_2	SEQ ID NO:	1470	Len:	100	Check:	8119	Weight:	1.00
Name:	00BW0874_2	SEQ ID NO:	1471	Len:	100	Check:	7661	Weight:	1.00
Name:	00BW1471_2	SEQ ID NO:	1472	Len:	100	Check:	6614	Weight:	1.00
Name:	00BW1616_2	SEQ ID NO:	1473	Len:	100	Check:		Weight:	1.00
Name:	00BW1686_8	SEQ ID NO:	1474	Len:	100	Check:		Weight:	1.00
Name:	00BW1759_3	SEQ ID NO:	1475	Len:	100	Check:	6894	Weight:	1.00
Name:	00BW1773_2	SEQ ID NO:	1476	Len:	100	Check:	7772	Weight:	1.00
Name:	00BW1783_5	SEQ ID NO:	1477	Len:	100	Check:	7149	Weight:	1.00
Name:	00BW1795_6	SEQ ID NO:	1478	Len:	100	Check:	7614	Weight:	1.00
Name:	00BW1811_3	SEQ ID NO:	1479	Len:	100	Check:	7968	Weight:	1.00
Name:	00BW1859_5	SEQ ID NO:	1480	Len:	100	Check:	6222	Weight:	1.00
Name:	00BW1880_2	SEQ ID NO:	1481	Len:	100	Check:	6941	Weight:	1.00
Name:	00BW1921_1	SEQ ID NO:	1482	Len:	100	Check:	8183	Weight:	1.00
Name:	00BW2036_1	SEQ ID NO:	1483	Len:	100	Check:	8175	Weight:	1.00
Name:	00BW2063 6	SEQ ID NO:	1484	Len:	100	Check:	8705	Weight:	1.00
Name:	00BW2087 2	SEQ ID NO:	1485	Len:	100	Check:	7388	Weight:	1.00
Name:	00BW2127 2	SEQ ID NO:	1486	Len:	100	Check:	8282	Weight:	1.00
Name:	00BW2128 3	SEQ ID NO:	1487	Len:	100	Check:	1723	Weight:	1.00
Name:	00BW2276 7	SEQ ID NO:	1488	Len:	100	Check:	6468	Weight:	1.00
Name:	00BW3819 3	SEQ ID NO:	1489	Len:	100	Check:	5670	Weight:	1.00
Name:	00BW3842 8	SEQ ID NO:	1490	Len:	100	Check:	7788	Weight:	1.00
Name:	00BW3871 3	SEQ ID NO:	1491	Len:	100	Check:	8574	Weight:	1.00
Name:	00BW3876 9	SEQ ID NO:	1492	Len:	100	Check:	7285	Weight:	1.00
Name:	00BW3886 8	SEQ ID NO:	1493	Len:	100	Check:	6446	Weight:	1.00
Name:	00BW3891 6	SEQ ID NO:	1494	Len:	100	Check:	8629	Weight:	1.00
Name:	00BW3970 2	SEQ ID NO:	1495	Len:	100	Check:	7113	Weight:	1.00
Name:	00BW5031 1	SEQ ID NO:	1496	Len:	100	Check:	5511	Weight:	1.00
Name:	96BW01B21	SEQ ID NO:	1497	Len:	100	Check:	7551	Weight:	1.00
Name:	96BW0407	SEQ ID NO:	1498	Len:	100	Check:	8226	Weight:	1.00
Name:	96BW0502	SEQ ID NO:	1499	Len:	100	Check:	8242	Weight:	1.00
Name:	96BW06 J4	SEQ ID NO:	1500	Len:	100	Check:	7544	Weight:	1.00
Name:	96BW11 06	SEQ ID NO:	1501	Len:	100	Check:	7942	Weight:	1.00
Name:	96BW1210	SEQ ID NO:	1502	Len:	100	Check:	8580	Weight:	1.00
Name:	96BW15B03	SEQ ID NO:	1503	Len:	100	Check:	7308	Weight:	1.00
Name:	96BW16 26	SEQ ID NO:	1504	Len:	100	Check:	7009	Weight:	1.00
Name:	96BW17A09	SEQ ID NO:	1505	Len:	100	Check:	6492	Weight:	1.00
Name:	96BWM01 5	SEQ ID NO:	1506	Len:	100	Check:	5837	Weight:	1.00
Name:	96BWMO3 2	SEQ ID NO:	1507	Len:	100	Check:	5277	Weight:	1.00
Name:	98BWMC12 2	SEQ ID NO:	1508	Len:	100	Check:	7807	Weight:	1.00
Name:	98BWMC13 4	SEQ ID NO:	1509	Len:	100	Check:	9051	Weight:	1.00
Name:	98BWMC14 a		1510	_	100	Check:	7867	Weight:	1.00
Name:			1511		100	Check:		Weight:	1.00
Name:			1512		100	Check:	7638	Weight:	1.00
Name:			1513		100	Check:	7495	Weight:	1.00
Name:			1514		100	Check:		Weight:	1.00
Name:	_			Len:	100	Check:		Weight:	1.00
Name:				Len:	100	Check:		Weight:	1.00
Name:	_		1517		100	Check:		Weight:	1.00
Name:			1518		100	Check:	6856	Weight:	1.00
Name:	_			Len:	100	Check:		Weight:	1.00
walle.		<u></u>						3	

SEQ ID NO		1				50
1469	00BW0762_1	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	SLGQHIYNTY
1470	00BW0768_2	MEQAPEDQGP	QREPYNEWTL	EILEELKQEA	VRHFPRPWLH	NLGEYIYETY
1471	00BW0874_2	MEQPPEDQGP	QREPYNEWTL	EILEELKQEA	VRHFPRPWLH	SLGQYIYETY
1472	00BW1471_2	MEQPPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	SLGQHIYETY
1473	00BW1616_2	MEQPPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	SLGQYIYENY
1474	00BW1686_8	MEQAPEDQGP	QREPYNEWAL	EILEELKQEA	VRHFPRPWLH	SIGQYIYETY
1475	00BW1759_3	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	GLGQHIYETY
1476	00BW1773_2	MEQPPEDQGP	QREPYNEWTL	ELLEELIQEA	VRHFPRPWLH	SLGQYIYETY
1477	00BW1783_5	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	SMGQHIYNTY
1478	00BW1795_6	MEQAPEDQGP	QREPYN.ETL	ELLEELKQEA	VRHFPRIWLH	NLGQYIYNTY
1479	00BW1811_3	MEQPPEDQGP	QRVPYNEWAL	ELLEELKQEA	VRHFPRPWLH	GLGQYVYETY
1480	00BW1859_5	MEQPPEDQGP	QREPYNEWAL	EILEELKQEA	VRHFPRLWLH	SLGQYIYETY
1481	00BW1880_2	MEQAPEDQGP	QRELYNEWTL	ELLEELKQEA	ARHFPSSWLH	GLGQHIYNTY
1482	00BW1921_1	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRTWLH	NLGQYIYQTY
1483	00BW2036_1	MEQAPEDQGP	QREPYNEWTL	EILEELKQEA	VRHFPRPWLQ	SLGQYIYETY
1484	00BW2063_6	MEQPPEDQGP	QREPYNEWTL	GLLEELKQEA	VRHFPRLWLH	NLGQYIYNTY
1485	00BW2087_2	MEQAPEDQGP	QREPYNEWAL	ELLEELKQEA	VRHFPRPWLH	NLGQYIYETY
1486	00BW2127_2	MEQAPEDQGP	QRGPYNEWTL	EILEELKQEA	VRHFPRPWLH	NLGQYIYETY
1487	00BW2128_3	MEQPPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	GLGQYIYETY
1488	00BW2276_7	MEQTPEDQGP	QREPYNEWAL	EILEELKQEA	VRHFPRTWLH	SLGQYIYDTY
1489	00BW3819_3	MEQAPEDQGP	QREPYNEWTL	EILEELKQGA	VRHFPRPWLH	NLGQHIYETY
1490	00BW3842_8	MEQVPEDQGP	QREPYNEWTL	EILEELKQEA	VRHFPRPWLQ	GLGHYIYETY
1491	00BW3871_3	MEQVPEDQGP	QREPYNEWTL	EILEELKQEA	VRHFPRPWLH	NLGQYIYETY
1492	00BW3876_9	MEQSPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	GIGQYIYETY
1493	00BW3886_8	MEQFPEDQGP	QREPYNEWTL	ELLEELKQEA	VKHFPRPWLH	NLGQHIYETY
1494	00BW3891_6	MEQPPEDQGP	QREPYNEWTL	EVLEELKQEA	VRHFPRPWLH	SLGQYVYETY
1495	00BW3970_2	MEQPPEDQGP	QREPYNEWAL	EILEELKQEA	VRHFPRPWLH	SLGQHIYETY
1496	00BW5031_1	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	SLGQHIYETY
1497	96BW01B21	MERPPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	GLGQYIYETY
1498	96BW0407	MERAPEDQGP	QREPYNEWAL	ELLEELKQEA	VRHFPRMWLH	GLGQYIYETY
1499	96BW0502	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPGPWLH	GLGQYVYETY
<u>1500</u>	96BW06_J4	MEQAPEDQGP	QREPYNEWTL	EILEELKQEA	VRHFPPPWLH	SLGQYIYETY
<u>1501</u>	96BW11_06	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	SLGQHIYNTY
<u>1502</u>	96BW1210	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	SLGQYIYETY
<u>1503</u>	96BW15B03	TEQAPEDQGP	QREPYNEWAL	EILEELKQEA	VRHFPRPWLH	SLGQYIYETY
1504	96BW16_26	MEQPPEDQGP	QREPYTEWAL	ELLEELKQEA	VRHFPRPWLH	GLGQYIYDTY
1505	96BW17A09	MEQTPEDQGP	QREPHNEWTL	ELLEELKQEA	VRHFPRPWLH	SLGQHIYETY
<u>1506</u>	96BWMO1_5	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPR.TLH	DLGQHIYNTY
1507	96BWMO3_2	MEQAPEDQGP	QREPYNEWTL	EILEELKQEA	IRHFPIPYLQ	HLGQYIYETY
1508	98BWMC12_2	MEQPPEDQGP	QREPYNEWTL	EILEELKQEA	VRHFPRPWLH	SLGQYIYETY
1509	98BWMC13_4	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRIWLH	NLGQYVYNTY
1510	98BWMC14_a	MEQAPEDQGP	QREPYNEWTL	EILEELKQEA	VRHLPRPWLH	SLGQHIYETY
<u>1511</u>	98BWM014_1	MEQAPEDQGP	QREPYNEWTL	ALLEDLKQEA	VRHVPRPWLH	SLGQHIYETY
1512	98BWM018_d	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPRPWLH	SLGQYIYETY
<u>1513</u>	98BWMO36_a	MEQAPEDQGP	QREPYNEWTL	ELLEELKQEA	VRHFPITWLH	NLGQYIYETY
<u>1514</u>	98BWM037_d	MEQAPEDQGP	QREPYNEWTL	EILEELKQEA	VRHFLRPWLH	DLGQYIYETY

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99BW3932_1 MEQAPEDQGP QREPYNEWTL EILEELKQEA VRHFPRPWLH NLGQYIYATY
1515
              99BW4642 4 MEQPPEDQGP QREPYNEWAL EILEELKQEA VRHFPRPWLH NLGQYIYETY
1516
              99BW4745 8 MEQPPEDQGP QREPYNEWTL EVLEDLKQEA VRHFPRPWLH SIGQYVYSTY
1517
              99BW4754_7 MEQAPENQGP QREPYNEWAL ELLEELKQEA VRHFPRPWLH DLGQHIYNTY
1518
              99BWMC16_8 MEQAPEDQGP QREPYNEWTL ELLEELKQEA VRHFPRPWLH SLGLYIYETY
1519
00BW0762 1 GDTWTGVEAI IRILQQLLFI HFRIGCQHSR IGIMRQ.... RRTRNGASRS
00BW0768 2 GDTWTGVEAL IRVLQQLLFI HFRIGCSHSR IGIVRQ.... RRARNGSSRS
00BW0874 2 GDTWTGVETI IRTLQQLLFI HFRIGCQHSR IGILRQ.... KRARNGASRS
00BW1471 2 GDTWAGVEAL LRILQQLLFI HFRIGCQHSR IGIIPQ.... RRARNGSRRS
00BW1616_2 GDTWAGVEAI TRILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGANRS
00BW1686_8 GDTWTGVEAL MRILQQLLFI HFRIGCQHSR IGILQR.... R.ARNGASRS
00BW1759 3 GDTWTGVEAI IRILQQLLFI HYRIGCQHSR IGIVRQ.... RRARNGANRS
00BW1773 2 GDTWTGVEAI IKILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGASRS
00BW1783 5 GDTWAGVEAI IRILQQLLFI HFRIGCQHSR IGILRQ.... RRTRNGASRS
00BW1795 6 GDTWTGVEAI IRTLQQLLFV HFRIGCQHSR IGIMRQ.... RRARNGTSGS
00BW1811_3 GDTWTGVEAI IRILQQLLFV HFRIGCQHSR IGILQQ.... RRARNGASRS 00BW1859_5 GDTWAGVEAL IRILQQLLFI HFRIGCQHSR IGILQQ.... RRARNGASRS
00BW1859_5 GDTWAGVEAL IRILQQLLFI HFRIGCQHSR IGILQQ.... RRARNGASRS
00BW1880_2 GDTWTGVEVL IRILQQLLFI HFRIGCQHSR IGIIRQ.... RRTRNGASRP
00BW1921_1 GDTWTGVEAL IRILQQLLFI HFRIGCQHSR IGITLP.... RRARNGANRS
00BW2036_1 GDTWTGVEAL IRILQQLLFI HFRIGCQHSR IGILQ.... RRARNGASRS
00BW2063_6 GDTWTGVEAL IRILQQLLFI HFRIGCQHSR IGIIRQ.... RRTRNGDSRS
00BW2087_2 GDTWTGVEAL IRILQQLLFT HYRFGCQHSR IGILQQ.... RRARNGANRS 00BW2127_2 GDTWTGVEVI IRILQQLLFI HFRIGCQHSR IGILRQ.... RRTRNGASRS
00BW2128_3 GDTWAGVESL IRMLQHLLFI HFRIGCQHSR IDX......
00BW2276_7 GDTWAGVEAI IRILQQLLFT HFRIGCHHSR IGILRQ.... RRARNGASRS
00BW3819 3 GDTWAGVEAL LRILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGASRP
00BW3842 8 GDTWTGVETI IRILQQLLFI HFRIGCSRSR IGPMRQ.... RRARNGASRS
00BW3871_3 GDTWTGVEAL LRVLQQLLFV HFRIGCQHSR IGILQQ.... RRARNGSSRS
00BW3876_9 GDTWTGVEAI IRILQQLLFI HYRIGCAHSR IGIVRQ.... RRARNGANRS
00BW3886 8 GDTWTGVEAI IRMLQQLLFI HFRIGCQHSR IGILRQ.... RRARNGANRS
00BW3891 6 GDTWTGVEAL IRMLQQLLFI HFKIGCQHSR IGILRR.... RRARNGASRS
00BW3970 2 GDTWTGVEAL IRILQQLLFI HFRIGCQHSR IGIILQ.... RRTRNGASRS
00BW5031 1 GDTWMGVEAL IRILQ..... HFRIGCQHSR IGIILQ.... RRTRNGASRS
 96BW01B21 GDTWTGVENM IRILQQLLFV HFRIGCQHSR IGILQQ.... RRARNGASRS
  96BW0407 GDTWTGVEAL IRTLQQLLFI HFRIGCQHSR IGILRQ.... RRVRNGTNRS
  96BW0502 GDTWTGVETL IRILQQLLFI HFRIGCQHSR IGILRQ.... RRTRNGASRS
 96BW06 J4 GDTWTGVETI IRILQQLLFI HFRIGCQHSR IGILQQ.... RRARNGASRP
 96BW11 06 GDTWTGVEAI IRILQQLLFI HFRIGCQHSR IGIIRQ.... RRTRNGASRP
  96BW1210 GDTWTGVEVL TRILQQLLFI HFRIGCQHSR IGILRQ.... RRTRNGASRS
 96BW15B03 GDTWTGVEAI IRILQQLLFI HFRIGCLHSR IGIMRQ.... RRARNGASRS
 96BW16 26 GDTWTGVEIK IRILQQLLFI HFRIGCQHSR IGILQQ.... RRARNGARRS
 96BW17A09 GDTWAGVEAL LRILQQLLFI HFRIGCHHSR IGITPQ.... RRARNGSRRS
 96BWMO1 5 GDTWTGVEAI TRILQQLLFI HYRIGCQHSR IGIMRQ.... RRARNGASRS
 96BWMO3 2 GDTWAGVLAI IRILQQLLFI HFRIGCSHSR IGIWR..... RRARNGASRS
98BWMC12 2 GDTWTGVEAI LRILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGASRS
98BWMC13 4 GDTWTGVEAI IRILQQLLFI HFRIGCQHSR IGILRQ.... RRTRNGASRS
98BWMC14_a GDTWTGVEAI IRILQQLLFI HFRIGCQHSR IGILPR.... RRARNGSSRS
98BWMC14_a GDTWTGVEAI IRILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGSSRS
98BWMO14_1 GDTWTGVEAI IRILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGANRS
98BWMO18_d GDTWTGVEVI IRILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGANRS
98BWMO36_a GDTWTGVEAL IRTLQQLLFI HFRIGCQHSR IGILRQ.... RRARNGASRS
98BWMO37_d GDTWTGVETI IRVLQQLLFI HFRIGCCHSR IGIVRQ.... RRARNGASRS
99BW3932_1 GDTWMGVEAL LRILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGASRS
99BW4642_4 GDTWAGVEAI IRVLQQLLFI HFRIGCHHSR IGIMQQ.... RRARNGASRS
99BW4745_8 GDTWTGVEAL MRILQQLLFI HFRIGCHHSR IGILRQ.... RGARNGASRS
99BW4754_7 GDTWTGVEAI IRILQQLLFI HFRIGCHHSR IGIIRQ.... RRTRNGASRP
99BWMC16 8 GDTWTGVEVI IRILQQLLFI HFRIGCQHSR IGILRQ.... RRARNGPSRS
```

Table 19. HIV Vpu Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

Name:	00BW0762_1		Len:	106	Check:		Weight:	1.00
Name:	00BW0768_2	SEQ ID NO: 152		106	Check:	7115	Weight:	1.00
Name:	00BW0874_2	SEQ ID NO: 152	Len:	106	Check:	7209	Weight:	1.00
Name:	00BW1471_2	SEQ ID NO: 152	Len:	106	Check:		Weight:	1.00
Name:	00BW1616 2	SEQ ID NO: 152	Len:	106	Check:	3870	Weight:	1.00
Name:	00BW1686_8	SEQ ID NO: 152	Len:	106	Check:	8787	Weight:	1.00
Name:	00BW1759 3	SEQ ID NO: 152	Len:	106	Check:	7584	Weight:	1.00
Name:	00BW1773 2	SEQ ID NO: 156	_	106	Check:	7507	Weight:	1.00
Name:	00BW1783 5	SEQ ID NO: 156	_	106	Check:	7874	Weight:	1.00
Name:	00BW1795 6	SEQ ID NO: 156	_	106	Check:		Weight:	1.00
Name:	00BW1735_8	SEQ ID NO: 157	_	106	Check:		Weight:	1.00
Name:	00BW1811_5	SEQ ID NO: 157	_	106	Check:		Weight:	1.00
	00BW1839_3	SEQ ID NO: 157	_	106	Check:	5827	Weight:	1.00
Name:	-	SEQ ID NO: 157	_	106	Check:		Weight:	1.00
Name:	00BW1921_1				Check:		Weight:	1.00
Name:	00BW2036_1	SEQ ID NO: 157		106			-	1.00
Name:	00BW2063_6	SEQ ID NO: 157	_	106	Check:		Weight:	
Name:	00BW2087_2	SEQ ID NO: 157	_	106	Check:	9545	Weight:	1.00
Name:	00BW2127_2	SEQ ID NO: 157	_	106	Check:	4898	Weight:	1.00
Name:	00BW2276_7	SEQ ID NO: 157	_	106	Check:	7311	Weight:	1.00
Name:	00BW3819_3	SEQ ID NO: 157		106	Check:	4879	Weight:	1.00
Name:	00BW3842_8	SEQ ID NO: 158	<u> Len </u>	106	Check:		Weight:	1.00
Name:	00BW3871_3	SEQ ID NO: 158	<u>l</u> Len:	106	Check:	6650	Weight:	1.00
Name:	00BW3876_9	SEQ ID NO: 158	Len:	106	Check:	6684	Weight:	1.00
Name:	00BW3886 8	SEQ ID NO: 158	B Len:	106	Check:	8701	Weight:	1.00
Name:	00BW3891 6	SEQ ID NO: 158	Len:	106	Check:	8544	Weight:	1.00
Name:	00BW3970 2	SEQ ID NO: 158	Len:	106	Check:	9375	Weight:	1.00
Name:	00BW5031 1	SEQ ID NO: 158	Len:	106	Check:	7778	Weight:	1.00
Name:	96BW01B21	SEQ ID NO: 158	Len:	106	Check:	6481	Weight:	1.00
Name:	96BW0407	SEQ ID NO: 158	E Len:	106	Check:	4225	Weight:	1.00
Name:	96BW0502	SEQ ID NO: 158	- 9 Len:	106	Check:	5292	Weight:	1.00
Name:	96BW06 J4	SEQ ID NO: 159	-	106	Check:	5367	Weight:	1.00
Name:	96BW11 06	SEQ ID NO: 159	_	106	Check:	6477	Weight:	1.00
Name:	96BW1210	SEQ ID NO: 159	_	106	Check:		Weight:	1.00
Name:	96BW15B03	SEQ ID NO: 159	_	106	Check:		Weight:	1.00
Name:	96BW16 26	SEQ ID NO: 159	_	106	Check:		Weight:	1.00
	96BW17A09	SEQ ID NO: 159	_	106	Check:		Weight:	1.00
Name:			_	106	Check:	5954	Weight:	1.00
Name:	96BWMO1_5		_		Check:	6334	Weight:	1.00
Name:	96BWM03_2	SEQ ID NO: 159	_	106			_	
Name:	98BWMC12_2	SEQ ID NO: 159	_	106	Check:		Weight:	1.00
Name:	98BWMC13_4	SEQ ID NO: 159	_	106	Check:	7458	Weight:	
Name:	98BWMC14_a		_	106	Check:		Weight:	1.00
Name:	_		_		Check:		Weight:	1.00
Name:	_		_		Check:		Weight:	1.00
Name:	98BWMO36_a		_		Check:		Weight:	1.00
Name:	98BWM037_d		4 Len:		Check:		Weight:	1.00
Name:	99BW3932_1		5 Len:		Check:		Weight:	1.00
Name:	99BW4642_4	SEQ ID NO: 156	6 Len:	106	Check:	8891	Weight:	1.00
Name:	99BW4745_8	SEQ ID NO: 156	7 Len:	106	Check:	3424	${\tt Weight:}$	1.00
Name:	99BW4754 7	SEQ ID NO: 156	B Len:	106	Check:	5468	Weight:	1.00
Name:	_		E Len:	106	Check:	6656	Weight:	1.00
Name:	A2 CD 97CD		Len:	106	Check:	6086	Weight:	1.00
	A2 CY 94CY		Len:		Check:	4609	Weight:	1.00
Name:			Len:		Check:		Weight:	1.00
	A2G CD 97C		- 3 Len:		Check:	4405	Weight:	1.00
	A BY 97BL0		Len:		Check:		Weight:	1.00
Name:			5 Len:		Check:		Weight:	1.00
		22g 12 110. 137		_ • •				

```
Check: 4192
                                                           Weight:
                                                                      1.00
Name: A SE SE659 SEQ ID NO: 1576 Len: 106
                                             Check: 3244
                                                           Weight:
                                                                      1.00
Name: A SE SE725 SEQ ID NO: 1577 Len: 106
                                             Check: 1918
                                                           Weight:
                                                                      1.00
Name: A SE SE753 SEQ ID NO: 1578 Len: 106
                                                                      1.00
                                                           Weight:
Name: A SE SE853 SEQ ID NO: 1579 Len: 106
                                             Check: 5495
                                                           Weight:
                                                                      1.00
Name: A SE SE889 SEQ ID NO: 1580 Len: 106
                                             Check: 5422
Name: A SE UGSE8 SEQ ID NO: 1581 Len: 106
                                             Check: 4254
                                                           Weight:
                                                                      1.00
                                             Check: 4081
                                                           Weight:
                                                                      1.00
Name: A_UG_92UG0 SEQ ID NO:
                             1582 Len: 106
Name: A_UG_U455_ <u>SEQ ID NO: 1583</u> Len: 106
Name: AC_IN_2130 <u>SEQ ID NO: 1584</u> Len: 106
                                                           Weight:
                                                                      1.00
                                             Check: 2987
                                             Check: 7929
                                                           Weight:
                                                                      1.00
Name: AC RW 92RW SEQ ID NO: 1585 Len: 106
                                             Check: 5133
                                                           Weight:
                                                                      1.00
Name: AC SE SE94 SEQ ID NO: 1586 Len: 106
                                             Check: 7394
                                                           Weight:
                                                                      1.00
                                             Check: 1852
Name: ACD SE SE8 SEQ ID NO: 1587 Len: 106
                                                           Weight:
                                                                      1.00
Name: ACG BE VII SEQ ID NO: 1588 Len: 106
                                             Check: 6357
                                                           Weight:
                                                                      1.00
Check: 5734
                                                           Weight:
                                                                      1.00
                                                           Weight:
                                                                      1.00
Name: AD_SE_SE71 SEQ ID NO: 1590 Len: 106
                                             Check: 4697
                                                                      1.00
Name: ADHK_NO_97 SEQ ID NO: 1591 Len: 106
                                             Check: 6301
                                                           Weight:
Name: ADK_CD_MAL SEQ ID NO: 1592 Len: 106
                                             Check: 4338
                                                           Weight:
                                                                      1.00
Name: AG_BE_VI11 SEQ ID NO: 1593 Len: 106
                                             Check: 3500
                                                           Weight:
                                                                      1.00
Name: AG_NG_92NG SEQ ID NO: 1594 Len: 106
                                             Check: 4859
                                                           Weight:
                                                                      1.00
                                                           Weight:
                                                                      1.00
Name: AGHU_GA_VI SEQ ID NO: 1595 Len: 106
                                             Check: 6173
Name: AGU_CD_Z32 SEQ ID NO: 1596 Len: 106
                                             Check: 9411
                                                           Weight:
                                                                      1.00
Name: AJ_BW_BW21 SEQ ID NO: 1597 Len: 106
                                             Check: 6158
                                                           Weight:
                                                                      1.00
Name: B AU_VH_AF SEQ ID NO: 1598 Len: 106
                                             Check: 5007
                                                           Weight:
                                                                      1.00
                                                           Weight:
                                                                      1.00
Name: B_CN_RL42_ SEQ_ID_NO: 1599 Len: 106
                                             Check: 4249
Name: B DE D31 U SEQ ID NO: 1600 Len: 106
                                             Check: 4572
                                                           Weight:
                                                                      1.00
                                                                      1.00
Name: B DE HAN U SEQ ID NO: 1601 Len: 106
                                             Check: 6819
                                                           Weight:
                                                           Weight:
                                                                      1.00
Name: B FR HXB2 SEQ ID NO: 1602 Len: 106
                                             Check: 5240
                                                                      1.00
                                             Check: 5651
                                                           Weight:
Name: B GA OYI M SEQ ID NO: 1603 Len: 106
                                                           Weight:
                                                                      1.00
Name: B GB CAM1 SEQ ID NO: 1604 Len: 106
                                             Check: 5359
                                                                      1.00
Name: B GB GB8 A SEQ ID NO: 1605 Len: 106
                                             Check: 1955
                                                           Weight:
Name: B GB MANC SEQ ID NO: 1606 Len: 106
                                             Check: 6521
                                                           Weight:
                                                                      1.00
Name: B KR WK AF SEQ ID NO: 1607 Len: 106
                                             Check: 2320
                                                           Weight:
                                                                      1.00
Name: B NL 3202A SEQ ID NO: 1608 Len: 106
                                             Check: 4510
                                                           Weight:
                                                                      1.00
Name: B TW TWCYS SEQ ID NO: 1609 Len: 106
                                             Check: 5491
                                                           Weight:
                                                                      1.00
Name: B US BC LO SEQ ID NO: 1610 Len: 106
                                             Check: 3142
                                                           Weight:
                                                                      1.00
Name: B US DH123 SEQ ID NO: 1611 Len: 106
                                             Check: 4669
                                                           Weight:
                                                                      1.00
Name: B US JRCSF SEQ ID NO: 1612 Len: 106
                                             Check: 4070
                                                           Weight:
                                                                      1.00
Name: B_US_MNCG_ SEQ ID
                         NO: 1613 Len: 106
                                             Check: 3291
                                                           Weight:
                                                                      1.00
Name: B_US_P896_ SEQ_ID_NO: 1614 Len: 106
Name: B_US_RF_M1 SEQ_ID_NO: 1615 Len: 106
                                             Check: 2280
                                                           Weight:
                                                                      1.00
                                             Check: 3104
                                                           Weight:
                                                                      1.00
Name: B US SF2 K SEQ ID NO: 1616 Len: 106
                                             Check: 3857
                                                           Weight:
                                                                      1.00
                                             Check: 3817
Name: B US WEAU1 SEQ ID NO: 1617 Len: 106
                                                           Weight:
                                                                      1.00
Name: B_US_WR27_ SEQ ID NO: 1618 Len: 106
                                             Check: 3329
                                                           Weight:
                                                                      1.00
Name: B US YU2 M SEQ ID NO: 1619 Len: 106
                                             Check: 5184
                                                           Weight:
                                                                      1.00
Name: BF1_BR_93B <u>SEQ ID</u>
                         NO: 1620 Len: 106
                                             Check: 3243
                                                           Weight:
                                                                      1.00
Name: C_BR_92B
                  SEQ ID NO: 1621 Len: 106
                                             Check: 7645
                                                           Weight:
                                                                      1.00
Name: C_BW_96BW0 <u>SEQ ID NO: 1622</u> Len: 106
                                             Check: 5235
                                                           Weight:
                                                                      1.00
Name: C_BW_96BW1 <u>SEQ ID NO: 1623</u> Len: 106
                                             Check: 6477
                                                           Weight:
                                                                      1.00
Name: C_BW_96BW1 <u>SEQ ID NO: 1624</u> Len: 106
                                             Check: 6400
                                                           Weight:
                                                                      1.00
                                             Check: 2981
                                                           Weight:
                                                                      1.00
Name: C_BW_96BW1 <u>SEQ ID NO: 1625</u> Len: 106
                                             Check: 8303
                                                           Weight:
                                                                      1.00
Name: C_ET_ETH22 SEQ ID NO: 1626 Len: 106
Name: C_IN_93IN1 SEQ ID NO: 1627 Len: 106
                                             Check: 8376
                                                           Weight:
                                                                      1.00
Name: C_IN_93IN9 SEQ ID NO: 1628 Len: 106
                                             Check: 6231
                                                           Weight:
                                                                      1.00
Name: C IN 93IN9 SEQ ID NO: 1629 Len: 106
                                             Check: 7626
                                                           Weight:
                                                                      1.00
Name: C_IN_94IN1 <u>SEQ ID NO: 1630</u> Len: 106
                                             Check: 6889
                                                           Weight:
                                                                      1.00
                                             Check: 8199
                                                           Weight:
                                                                      1.00
Name: C IN 95IN2 SEQ ID NO: 1631 Len: 106
                                                           Weight:
                                                                      1.00
Name: CRF01_AE_C SEQ ID NO: 1632 Len: 106
                                             Check: 4437
                                                                      1.00
Name: CRF01_AE_C SEQ ID NO: 1633 Len: 106
                                             Check: 4082
                                                           Weight:
                                             Check: 3725
                                                           Weight:
                                                                      1.00
Name: CRF01_AE_C SEQ ID NO: 1634 Len: 106
Name: CRF01_AE_T SEQ ID NO: 1635 Len: 106
                                             Check: 3201
                                                           Weight:
                                                                      1.00
```

```
Weight:
                                                                  1.00
Name: CRF01 AE T SEQ ID NO: 1636 Len: 106
                                           Check: 3137
Name: CRF01 AE T SEQ ID NO: 1637 Len: 106
                                           Check: 3484
                                                        Weight:
                                                                  1.00
                                                                  1.00
Name: CRF01 AE T SEQ ID NO: 1638 Len: 106
                                           Check: 3491
                                                        Weight:
Name: CRF01 AE T SEQ ID NO: 1639 Len: 106
                                                                  1.00
                                           Check: 2300
                                                        Weight:
                                                        Weight:
                                                                  1.00
Name: CRF01_AE_T SEQ ID_NO: 1640 Len: 106
                                           Check: 2481
                                                        Weight:
                                                                  1.00
Name: CRF02 AG F SEQ ID NO:
                                           Check: 2748
                            1641 Len: 106
                                                        Weight:
                                                                  1.00
Name: CRF02 AG F SEQ ID NO:
                                           Check: 4618
                            1642 Len: 106
Name: CRF02 AG G SEQ ID NO:
                                           Check: 400
                                                        Weight:
                                                                  1.00
                            1643 Len: 106
                                           Check: 5979
                                                        Weight:
                                                                  1.00
Name: CRF02 AG N SEQ ID NO:
                            1644 Len: 106
                                           Check: 5296
                                                        Weight:
                                                                  1.00
Name: CRF02 AG S SEQ
                            1645 Len: 106
                     ID NO:
                                           Check: 4213
                                                        Weight:
                                                                  1.00
Name: CRF02 AG_S SEQ
                     ID NO:
                            1646 Len: 106
                            1647 Len: 106
                                           Check: 952
                                                        Weight:
                                                                  1.00
Name: CRF03_AB_R SEQ ID NO:
                                                        Weight:
                                                                  1.00
Name: CRF03_AB_R SEQ ID NO:
                            1648 Len: 106
                                           Check: 431
Name: CRF04_cpx_ SEQ ID NO:
                                                        Weight:
                                                                  1.00
                            1649 Len: 106
                                           Check: 6986
Name: CRF04_cpx_ <u>SEQ ID NO: 1650</u> Len: 106
                                           Check: 8606
                                                        Weight:
                                                                  1.00
                                           Check: 5826
                                                        Weight:
                                                                  1.00
Name: CRF04_cpx_ SEQ ID NO: 1651 Len: 106
                                           Check: 5193
                                                        Weight:
                                                                  1.00
Name: CRF05 DF B SEQ ID NO: 1652 Len: 106
Name: CRF05_DF_B SEQ ID NO: 1653 Len: 106
                                           Check: 5092
                                                        Weight:
                                                                  1.00
Name: CRF06_cpx_ SEQ ID NO: 1654 Len: 106
                                           Check: 3214
                                                        Weight:
                                                                  1.00
Name: CRF06_cpx_ SEQ ID NO: 1655 Len: 106
                                           Check: 3831
                                                        Weight:
                                                                  1.00
                                           Check: 4862
                                                        Weight:
                                                                  1.00
Name: CRF06_cpx_ SEQ ID_NO: 1656 Len: 106
                                                        Weight:
                                                                  1.00
Name: CRF06_cpx_ SEQ ID NO: 1657 Len: 106
                                           Check: 3114
Name: CRF11_cpx_ <u>SEQ ID NO: 1658</u> Len: 106
                                           Check: 4492
                                                        Weight:
                                                                  1.00
                                           Check: 9106
                                                                  1.00
Name: CRF11 cpx SEQ ID NO: 1659 Len: 106
                                                        Weight:
                                           Check: 5829
                                                        Weight:
                                                                  1.00
Name: D CD 84ZR0 SEQ ID NO: 1660 Len: 106
Name: D CD ELI K SEQ ID NO: 1661 Len: 106
                                           Check: 2669
                                                        Weight:
                                                                  1.00
Name: D CD NDK M SEQ ID
                        NO:
                            1662 Len: 106
                                           Check: 4007
                                                        Weight:
                                                                  1.00
                                                                  1.00
Name: D UG 94UG1 SEQ ID
                        NO:
                            1663 Len: 106
                                           Check: 2098
                                                        Weight:
Name: F1 BE VI85 SEQ ID
                            1664 Len: 106
                                           Check: 4208
                                                        Weight:
                                                                  1.00
                        NO:
                                           Check: 4525
                                                        Weight:
                                                                  1.00
Name: F1 BR 93BR SEQ ID
                        NO:
                            1665 Len: 106
                                                        Weight:
                                                                  1.00
Name: F1 FI_FIN9 SEQ
                     ID
                            1666 Len: 106
                                           Check: 5556
                        NO:
                                                        Weight:
                            1667 Len: 106
                                           Check: 4332
                                                                  1.00
Name: F1 FR MP41 SEQ
                     ID
                        NO:
                            1668 Len: 106
                                           Check: 5691
                                                        Weight:
                                                                  1.00
Name: F2 CM MP25 SEQ ID
                        NO:
Name: F2KU BE VI SEQ ID
                            1669 Len: 106
                                           Check: 4047
                                                        Weight:
                                                                  1.00
                        NO:
                                           Check: 3839
                                                        Weight:
                                                                  1.00
Name: G BE DRCBL SEQ ID
                        NO:
                            1670 Len: 106
                            1671 Len: 106
                                           Check: 825
                                                        Weight:
                                                                  1.00
Name: G NG 92NG0 SEQ ID
                        NO:
Name: G_SE_SE616 SEQ ID NO: 1672 Len: 106
                                           Check: 4456
                                                        Weight:
                                                                  1.00
Name: H BE VI991 SEQ ID NO: 1673 Len: 106
                                           Check: 2728
                                                        Weight:
                                                                  1.00
Name: H BE VI997 SEQ ID
                        NO: 1674 Len: 106
                                           Check: 3468
                                                        Weight:
                                                                   1.00
Name: H_CF_90CF0 SEQ ID NO: 1675 Len: 106
                                                        Weight:
                                                                  1.00
                                           Check: 5568
Name: J_SE_SE702 SEQ ID NO: 1676 Len: 106
                                           Check: 4413
                                                        Weight:
                                                                   1.00
Name: J_SE_SE788 SEQ ID NO: 1677 Len: 106
                                           Check: 3659
                                                        Weight:
                                                                   1.00
Name: K_CD_EQTB1 SEQ ID NO: 1678 Len: 106
                                           Check: 4999
                                                        Weight:
                                                                   1.00
                                           Check: 4729
                                                        Weight:
                                                                   1.00
Name: K_CM_MP535 SEQ ID
                        NO: 1679 Len: 106
                                           Check: 8961
                                                        Weight:
                                                                   1.00
Name: N_CM_YBF30 SEQ ID
                        NO: 1680 Len: 106
Name: O_CM_ANT70 SEQ ID
                        NO: 1681 Len: 106
                                           Check: 7210
                                                        Weight:
                                                                   1.00
                                                        Weight:
                                                                   1.00
Name: O_CM_MVP51 <u>SEQ ID NO: 1682</u> Len: 106
                                           Check: 8490
Check: 726
                                                        Weight:
                                                                   1.00
Check: 9615
                                                        Weight:
                                                                   1.00
Name: U CD 83C SEQ ID NO: 1685 Len: 106
                                           Check: 6063
                                                        Weight:
                                                                   1.00
SEQ ID NO
                      ......MI ELIAAVDYRI GVA.ALIIAL IIAIVVWTIA YIEYRKLLKQ
          00BW0762 1
1520
                      ......ML ELTARVDYRL GVG.ALIVAI ILAIVVWIWA YIEYKELLRQ
1521
          00BW0768 2
                      .....ML GLSEKAGYAL GVG.ALIVAL IIVIVVWTIV YIEYRKLVRQ
          00BW0874 2
1522
                      ......MI NLLERVDX.. GVG.ALGIAL IIVIVVWTIV YIEYRKLVRQ
1523
          00BW1471_2
                      00BW1616 2
1524
                      ...MEDVILS FIA.KIDYRI GIA.AIIVAL ILAIIVWTIV YLEYRKLVRQ
          00BW1686 8
1525
```

```
.....MID LSA.RVDYRI GVA.AFIIAL IIAIVVWTIV YIEYRKLLRQ
1526
         00BW1759 3
                   MLKLATIVDY ILAAKVDYRV GIG.ALIAAL IITIVVWIIV YREYRKLLRQ
1527
         00BW1773 2
                   ...IVDVIFS LTD.RVDYRI AVA.ALTIAL IIAIVVWTIV YIEYRKLVRQ
         00BW1783_5
1528
                    .....MVD WTKXKVDYRI AVV.AFIVAL IIAIVVWTIV YIEYRKLRKQ
         00BW1795 6
1529
                    00BW1811 3
1530
                    ......ML ELTARVDYRL GVG.ALIVAL IIAIIVWTIA SLEYRKLKRQ
1531
         00BW1859 5
                    .....MLS LMT.RVDYRI AVA.AFVIAL ILAIIVWTIA YLEYRKLVKQ
         00BW1880 2
1532
                    .....MLD LAA.IVDYRI TIV.AFAIAL FIAIIVWTIA YLEYRKLVRO
         00BW1921 1
1533
                    .....ML DLIAKVDYRV GIG.ALIVAL IIAVVVWIIA YIEYRKLLKQ
         00BW2036 1
1534
                    ......MID WTE.QVDYRI AIVXSFIVAL IIAIVIWTLA YIEYRKLSRQ
         00BW2063 6
1535
         00BW2087 2
                   .....ML SLIERIDYRL GVG.ALIVAL IIVIIVWTIV YIEYRKLVRQ
1536
                   .....ML DLAARVDYRL GVG.ALVVAL IIAIIVWTIV YIEYRKLVRQ
         00BW2127 2
1537
                    ......... M VDLGRVDYRL GVG.ALIVAL IIAIVVWIIV YIEYRKLVRQ
         00BW2276 7
1538
                    .....ML DLLTRVDYRL GVG.ALIVAL IIAIIVWTIA YIEYRKLLRQ
         00BW3819 3
1539
                    .....MF DLLAGVDYRL GVG.ALIIAL IIAIVVWVIA YIEYKKWLKQ
         00BW3842 8
1540
                   .....MVD LLE.KVDYRI GIA.AFTVAL LIAIIVWIIA YIEYRKLVRQ
         00BW3871 3
1541
                   ........M LDLTQIGYEL GIG.ALIVAL IIAIVVWTIV YIEYRKVLRQ
         00BW3876_9
1542
                    1543
         00BW3886 8
                    .....ML DLLAGVDYRI GVG.AFLVAL SIAIVVWTIV YIEYRKLLRQ
         00BW3891 6
1544
                    ......MF SLLERIDYRL GVG.ALLVAL IIAIVVWAIV YIEYRKLVRQ
1545
         00BW3970 2
                    ......... M FALFEVDYRL TIG.AFIVAL FLAIVVWTIA YLEYRKLVRQ
         00BW5031 1
1546
                    .....ML ELIAKIDYRL GGG.ALIVAL SIAIVVWIIA YIEYKKLIRQ
          96BW01B21
1547
                    .....ML SLAA.IDYRI GVG.AFVVAL IIAIIVWIIV YIEYRKLVRQ
1548
          96BW0407
                    .....MI NFLAKVDYRL GVG.ALIVAF IIAIVVWIIA YIEYRKLLRQ
          96BW0502
1549
                    .....MID LLA.RVDYRI GLA.AFVVAL LIAIIVWTIV YLEYRKLVRQ
          96BW06_J4
1550
                    .....MVD LLA.KVDYKI AVA.AFIIAL IIAIVVWIIV YVEYRKLVKQ
          96BW11_06
1551
                    .....ML YLLEKVDYRL GVG.ALIIAL IIAIIVWTIA YLEYRKVLRQ
1552
          96BW1210
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          96BW15B03
1553
          96BW16_26
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1554
                    .....ML NLLAKVDYRL GVG.ALVIAL IIAIVVWIIA YIEYRKLVRQ
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          96BW17A09
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<u>1556</u>
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1557
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         98BWMC12 2
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1561
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         98BWM018 d
1562
                    .....ML AFLARVDYRL GVG.AFIIAL IIAIIVWTIA YLEYRKLVRO
1563
         98BWM036 a
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         98BWM037 d
1564
                    1565
         99BW3932 1
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1567
                    99BW4754 7
1568
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1570
                    A2 CY 94CY
1571
                   1572
         A2D 97KR
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            1574
     A BY 97BL0
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     A KE Q23 A
1575
            1576
     A SE SE659
            1577
     A SE SE725
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     A SE SE753
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            .....MSA LEISALEIWS IVG..LVVAL ILAIVVWTIV GIECKRLQKQ
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     A SE SE889
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            1582
     A UG 92UG0
            A UG U455
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            AC IN 2130
1584
            AC RW 92RW
1585
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     AC SE SE94
1586
            ACD SE SE8
1587
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     ACG BE VI1
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     AD_SE_SE69
            1590
     AD SE SE71
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     ADHK NO_97
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     ADK_CD MAL
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            AG NG 92NG
1594
            AGHU_GA_VI
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     B AU VH AF
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1600
     B DE HAN U
            1601
            1602
     B FR HXB2
            B_GA_OYI_M
1603
            ..... ... MLPLQIA IVA..LVVVA IIAIVVWTIV FIEYRKIRRQ
     B GB CAM1
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            ...... IQILT IVA..LVVAG IVAIVVWIIV FIEYRKILKK
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     B GB GB8_A
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     B GB MANC
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1607
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     B_NL_3202A
            1609
     B TW_TWCYS
            B US BC LO
1610
            B US DH123
1611
            1612
     B US JRCSF
     B_US_MNCG
            1613
            B US P896_
1614
            B US RF M1
1615
            1616
     B US SF2 K
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     B US WEAU1
1617
            ..... ....MPLYILA VVA..LVLAA IIAIVVWTIV FIEYRKILRQ
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1619
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1624
      C BW 96BW1
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      C BW 96BW1
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      C ET ETH22
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      C IN 93IN9
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1629
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1630
      C IN 94IN1
              .............MVNLDYKL GVG.ALIVAL IIAIVVWTIV YIEYRKLVQQ
      C IN 95IN2
1631
              ........ ... MSALQIA IVG..LIVAL ILAIVVWTIV FIEYKKILRQ
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1632
              1633
      CRF01 AE C
              CRF01 AE C
1634
              1635
      CRF01 AE T
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1636
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      CRF01 AE T
1637
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      CRF01 AE T
              1639
              CRF01_AE_T
1640
              CRF02 AG F
1641
      CRF02 AG F
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1642
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1643
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              1644
      CRF02 AG N
      CRF02 AG S
              1645
              1646
      CRF02 AG_S
              CRF03 AB R
1647
      CRF03 AB R
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              1649
      CRF04 cpx
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      CRF05 DF B
              ...... .... MSDLLA VAIAAFIVAL IIAIVVWTIV YLEYRKLVRQ
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              1655
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              1659
      CRF11_cpx_
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      D CD NDK M
              1663
      D UG 94UG1
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              ....... .... MSNLLA IGIAALIVAL IITIVVWTIA YIEYKKLVRQ
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1666
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        F2 CM MP25
1668
                  ...... MNL.LL VGIGALIVAF LLAIVVWTIA YLEYRKVLKQ
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1669
                  G BE DRCBL
1670
                  G NG 92NG0
1671
                  G SE SE616
1672
                  ...... ....MNILGI GIG.ALVVAF IIAIVVWTIA YIEYRKLK.Q
        H BE VI991
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                  ..... MYIIGI GIG.ALIVAF IIAIVVWTIV YIEYRKLVKQ
        H BE VI997
1674
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        H CF 90CF0
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        J SE SE702
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        J SE SE788
1677
                  K CD EQTB1
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        N CM YBF30
1680
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        O CM ANT70
                  O CM MVP51
1682
                  O SN 99SE
1683
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1684
        U CD 83C
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1685
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         KNIDW....L IKRIRERAED SGNESEGD.T EEL....ATM VDMGHLRLLD
 96BW15B03
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            RRIDO....L IKRIGERAED SGNESDGD.T EEL....STL VDMGHLRLLD
98BWMC12 2
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98BWMC13 4
            RKIDW....L IERIRERAED SGNESEGD.T EEL....ATM VDMGQLRLLD
98BWMC14 a
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98BWM014 1
98BWM018 d
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99BW3932<sup>-</sup>1
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            NKIDW....L IKRISERAED SGNESEGD.T EEL....STL MEMGNLDFGD
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AD SE SE71
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            KKIEK....L PDRIRERAED SGNESEGD.T DEL....ATL VERGNFDPWV
AG BE VI11
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            KQVDR....L IDRIIERAED SGNESEGD.Q EEL....SAL MEMGHNAPWD
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B US_JRCSF
            RKIDR....L IDRISERAED SGNESEGD.Q EEL....SAL VGMGHDAPWV
B US MNCG
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B US RF M1
B US SF2 K
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B US YU2 M
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C BR 92BR0
            RRIDW....L VKRIKERAED SGNESGGD.T EEL....ETM VDMGHLRLLD
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BW_96BW1
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CRF01 AE T
CRF01 AE T
            RKIDR....L VKRIRERAED SGNESEGD.T DEL....AKL VEMGDFDPWV
CRF01 AE T
            RKIDR....L IKRIGERAED SGNESEGD.T DEL....AKL VEMGDFDPWV
            KKIDK....L LDRIRERAED SGNESDGD.A EEL....STL MEMGYD.HIL
CRF02 AG F
            KKIDK....L LDRIRERAED SGNESDGD.T EEL....STL LEMGYD.NIL
CRF02 AG F
            KKIDK....L LDRIREREED SGNESEGD.A EEL....SKL MEMGHD.FWI
CRF02 AG G
            KKIDR....L LDRIRERAED SGNESDGD.T EEL....STL MEMGYE.YIL
CRF02 AG N
            KKIDR....L LDRIRERAED SGNESDGD.T EEL....STL MEMGYD.NIL
CRF02 AG S
            GKIDK....L LDRIRERAED SGNESDGD.T EEL....STL LEMGYDNAAL
CRF02 AG S
            RKIDR....L IDRIRERAED SGNESEGD.Q E......AL MEMGHLVPWD
CRF03 AB R
            RKIDR....L IDRIRERAED SGNESEGD.Q E......AL MEMGHLAPWD
CRF03 AB R
            RRIDS....L YNRIRERAED SGNESDGD.A EEL....STL VGMGNFDPWV
CRF04 cpx
            RKIDR....L YKRIRERAED SGNESDGD.T EEL....STL VGMGDFDPWV
CRF04 cpx
            RKIDR....L CKRIIERAED SGNDSDGD.T EEL....STL VDMGDFHPLV
CRF04 cpx
            RKINR....L YKRIRERAED SGNESEGD.A EEL....AAL GEVGPFIPGD
CRF05 DF B
CRF05_DF_B
            RKINR....L YKRIRERAED SGNESEGD.A EEL....AAL GEMGPFIPGN
            KKIEK....L LDRIRERAED SGNESEGD.T DEL....ATL MEMGDFDPWV
CRF06_cpx_
            RKIEK....L LNRIRERAED SGNESEGD.T EEL....AAF MEMGNFDPWV
CRF06_cpx_
            KKIEK....L LDRIRERAED SGNESEGD.T DEL....ATL MEMGNFDPWV
CRF06_cpx_
            KKIEK....L LDRIREREED SGNDSEGD.T EEL....ATL MEMGNFDPWV
CRF06_cpx_
            KKIDR....L IDRIRERAED SGNESEGD.T EEL....ARL VEMGPHDQWN
CRF11_cpx_
            R.....K DRLRIRRAED SGNESEGD.T EEL....AQL VEMGPHDLWN
CRF11_cpx_
            RKIDW....L IDRIREREED SGNESEGDKE ELS....TL. VEMGHHAPWD
D_CD_84ZR0
D CD ELI K
            RRIDC....L LDRITERAED SGNESEGDRE KLS....KL. VEMGHHAPWD
            RKIDC....L IDRIRERAED SGNESEGERE ELS....KL. VEMGHHAPWD
D CD NDK M
            RKIDW....L IDRIRERAED SGNESEGDKE ELS....AL. VEMGHDAPWD
D UG 94UG1
            RKINK....L YKRIRERAED SGNESEGD.A EEL....AAL GEMGPFIPGD
F1_BE_VI85
            RKINR....L YKRISERAED SGNESEGD.A EEL....AAL GEVGPFIPGD
F1_BR_93BR
            RKINR....L YIRIRERAED SGNESEGD.A EEL....AAL GKMGPFIPGD
F1 FI FIN9
            RKINR....L YERIRERAED SGNESEGD.A EEL....AAL GEMGSFISGD
F1 FR MP41
            KRINR....L YERIIERAED SGNESEGD.A EEL....AAL GEVGPLIPGD
F2 CM MP25
            ERINQ....L YNRLIERAED SGNESEGE.A EEL....AAL GEVGHLVLGN
F2KU BE VI
            KRIEK....L LDRIRERAED SGNESEGD.T EEL....ATL MELGDFDPWV
G BE DRCBL
            KKIEK....L LDRIRERAED SGNESEGD.T EEL....ATL MEMGDFDPWV
G NG 92NG0
            KRIGK....L LDRIRERAED SGNESDGD.T EEL....VTL VEMGDFDPWV
G SE SE616
            RKIDR....L IERIRERAED SGNESDGD.T EEL....SKL VEMGHLNLGY
H BE VI991
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H BE VI997
            KKIDR....L IERIGERAED SGNESDGD.T EEL....SKL MEMGHLNLGY
H CF 90CF0
            RKIDK....L INRIRERAED SGNESDGD.T DEL....AEL VEMGPHDLWN
J SE SE702
            RKIDK....L IDRIRERAED SGNESDGD.T EEL....ADL VERGPHDLWN
J SE SE788
            KRINW....L FDRIRERAED SGNESEGD.T EEL....AAL GETGHLILGD
K CD EQTB1
            KRINW....L IDRIRERAED SGNESEGD.A EEL....ADI GELGHLILGN
K CM MP535
            EKIKH....I RQRIREREED SGNESDGD.A EWLDGDEEWL VTLLSSSKLD
N_CM_YBF30
O CM ANT70
            DRKEREILER LRRIREIRDD SDYESNGE.. EEQ.....EV MDLVLSHGFD
            DRREQEILER LRRIKEIRDD SDYESNEE.. EQQ.....EV MELIHSHGFA
O CM MVP51
O SN 99SE
            DKREREILER LRRIRQIEDD SDYESDGT.. EEQ.....EV RDLVHSYGFD
            DRREREILER LRRIRQIEDD SDYESDGK.. EEQ.....EV RDLVHGYGFD
O SN 99SE
            RKIDW....L IDRIRERAED SGNESEGD.T EEL....STL VEMEPDNFRN
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            ANGL..
00BW0768 2
            GNDL..
00BW0874_2
            VNDL..
00BW1471_2
            VNDL..
            DL...
00BW1616_2
00BW1686_8
            VNVL..
00BW1759_3
            DNNL..
00BW1773_2
            INH...
00BW1783_5
            AHDL..
00BW1795 6
            ANNL..
00BW1811_3
            IINY..
00BW1859 5
            INDL..
00BW1880 2
            ANDL..
00BW1921 1
            HGL...
00BW2036 1
            VHDL..
00BW2063 6
            ANDL..
00BW2087 2
            VNDL..
00BW2127 2
            DL...
00BW2276 7
            GNDL..
00BW3819 3
            AHDL..
00BW3842_8
            L....
00BW3871 3
            VNDI..
00BW3876 9
            INNL..
00BW3886 8
            VNNL..
00BW3891_6
            VNDV..
00BW3970_2
            VTDL..
00BW5031_1
            VNDL..
 96BW01B21
            DNAL..
  96BW0407
            DI...
  96BW0502
            VNN...
 96BW06_J4
            NL...
 96BW11_06
            ANDL..
  96BW1210
            ADGL..
 96BW15B03
            L....
 96BW16 26
            INN...
 96BW17A09
            VNDL..
 96BWM01_5
            TNDL..
 96BWMO3_2
            INL...
98BWMC12_2
            DNEL..
98BWMC13 4
            VNDL..
98BWMC14 a
            VM....
98BWMO14 1
            ANDL..
98BWM018 d
            ANDL..
98BWMO36 a
            AHDL..
98BWMO37_d ANDL..
99BW3932 1
            . . . . . .
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99BW4642 4
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99BW4745 8
             DL...
99BW4754 7
             VNDL..
99BWMC16_8
             ANDL..
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             DNDV..
A2_CY_94CY
A2D___97KR
             VNNV..
             AND...
A2G_CD_97C
             GDNL..
A BY 97BL0
             DNNV..
A_KE_Q23_A
             NNIL..
A_KE_Q23_A
A_SE_SE659
A_SE_SE725
A_SE_SE753
             DNNL..
             DNDL..
             GNNL..
A_SE_SE853
             DNNL..
A_SE_SE889
             NNNL..
A_SE_UGSE8
             DNNL..
A_UG_92UG0
             DNNL..
             DNNL..
A_UG_U455_
AC_IN_2130
             VNGL..
AC_RW_92RW
             VNNL..
AC_SE_SE94
             VNNL..
ACD_SE_SE8
             DINL..
ACG BE VI1
             AIDL..
AD SE SE69
             VDDM..
AD SE SE71
             DNNL..
ADHK NO 97
             VADL..
ADK CD MAL
              VDDL..
AG BE VI11
             GDNL..
AG_NG_92NG
             GDNL..
AGHU_GA_VI
             VNDL..
AGU_CD_Z32
             GDNL..
AJ_BW_BW21
             VNDL..
B_AU_VH_AF
              VDDL..
B_CN_RL42
              VDDL..
B_DE_D31_U
             VDDL..
B DE HAN U
              VNDQ..
B FR HXB2
              VDDL..
B_GA_OYI_M
              VDDM..
B GB CAM1
              VNDL..
B_GB_GB8_A
              VDDL..
B_GB_MANC
              VDDL..
B_KR_WK_AF
              VDDL..
B_NL_3202A
              VDDL..
              VNDQ..
B_TW_TWCYS
              IDDL..
B_US_BC_L0
B_US_DH123
              IDDL..
B_US_JRCSF
              INDL..
B_US_MNCG_
              INDL..
B_US_P896_
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              VDDL..
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B_US_SF2_K
              VDDL..
B_US_WEAU1
              IDDL..
B_US_WR27_
              VDDL..
B_US_YU2_M
              VDDL..
BF1 BR 93B
              IDNL..
C BR 92BR0
              GNDL..
C_BW_96BW0
              DN...
C_BW_96BW1
              ANDL..
C_BW_96BW1
              ADGL..
C BW_96BW1
             L....
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C ET ETH22
             VNDL..
C IN 93IN1
             VNDL..
C IN 93IN9
             VNDL..
C IN 93IN9
             VNDM..
C IN 94IN1
             VNDL..
C_IN_95IN2
             VNDL..
CRF01_AE_C
             GDNL..
CRF01_AE_C
             GDNL..
CRF01_AE_C
             GDNV..
CRF01_AE_T
CRF01_AE_T
             GDNL..
             GDNL..
CRF01_AE_T
             GDNV..
CRF01_AE_T
             GDNL..
CRF01_AE_T
             GDNL..
CRF01_AE_T
             GDNL..
CRF02_AG_F
             DNDNL.
CRF02_AG_F
             DNDNL.
CRF02_AG_G
             DNL...
CRF02_AG_N
             DNDNL.
             DNDNL.
CRF02_AG_S
CRF02_AG_S
             DIDNL.
CRF03_AB_R
             ADDL..
CRF03_AB_R
             ADDL..
             GDNL..
CRF04_cpx_
             GNNV..
CRF04_cpx_
CRF04 cpx
             GNNL..
CRF05 DF B
             INNL..
CRF05_DF_B
             INNL..
             GDNL..
CRF06_cpx_
CRF06_cpx_
             GDNL..
CRF06_cpx_
             GDNL..
CRF06_cpx_
             GDNL..
CRF11_cpx_
             VNDL..
CRF11_cpx_
             VNDL..
D_CD_84ZR0
             VDDDL.
D_CD_ELI_K
             IDDL..
D_CD_NDK_M
             VDDL..
D UG 94UG1
             ADDM..
F1_BE_VI85
             INNL..
F1_BR_93BR
             INNL..
F1 FI FIN9
             VNNL..
F1_FR_MP41
             INNL..
F2_CM_MP25
             INNL..
F2KU_BE_VI
             IHNL..
G_BE_DRCBL
             GDNL..
G_NG_92NG0
             GNNL..
G_SE_SE616
             GDNL..
H_BE_VI991
             VADL..
H_BE_VI997
             VADL..
             VADL..
H_CF_90CF0
             VNDL..
J_SE_SE702
J_SE_SE788
             VNDL..
K_CD_EQTB1
             INNL..
K_CM_MP535
             IDNL..
N_CM_YBF30
             QGNWV.
O CM_ANT70
             NPMFEP
O_CM_MVP51
             NPMFEL
O_SN_99SE_
             NPMFEL
O_SN_99SE_
             NPMFEP
U_CD___83C
             DNDM..
```

Table 20. BLASTP Sequences producing significant alignments with S20757 (HBV Polymerase subtype ayw) $\frac{1}{2}$

	Score (bits)	E: Value
gi 93080 pir S20757 DNA-directed DNA polymerase (EC 2.7.7	1553	0.0
gi 8925755 gb AAF81607.1 DNA polymerase/reverse transcript.		0.0
gi 1514497 emb CAA68864.1 P [Hepatitis B virus]	1488	0.0
gi 27466573 gb AAO12632.1 polymerase [Hepatitis B virus]	1482	0.0
gi 5257489 gb AAD41360.1 polymerase [Hepatitis B virus]	1482	0.0
gi 118876 sp P03156 DPOL_HPBVY P protein [Includes: DNA-dir.	1482	0.0
gi 27466565 gb AAO12625.1 polymerase [Hepatitis B virus]	1481	0.0
gi 67003 pir JDVLVB DNA-directed DNA polymerase (EC 2.7.7	1480	0.0
gi 59433 emb CAA46352.1 polymerase ORF [Hepatitis B virus]	1480	0.0
gi 6692498 gb AAF24666.1 polymerase [Hepatitis B virus]	1479	0.0
gi 6692505 gb AAF24673.1 polymerase [Hepatitis B virus]	1479	0.0
gi 2117935 pir S71785 DNA-directed DNA polymerase (EC 2.7	1477	0.0
gi 28436101 dbj BAC57445.1 polymerase [Hepatitis B virus]	1476	0.0
gi 631984 pir S47406 DNA-directed DNA polymerase (EC 2.7.7.		0.0
gi 1359687 emb CAA66431.1 polymerase [Hepatitis B virus]	1474	0.0
gi 18621117 emb CAC87021.1 polymerase [Hepatitis B virus]	1474	0.0
gi 28436091 dbj BAC57437.1 polymerase [Hepatitis B virus]	1473	0.0
gi 6692512 gb AAF24680.1 polymerase [Hepatitis B virus]	1472	0.0
gi 22135695 gb AAM09037.1 polymerase [Hepatitis B virus]	1471	0.0
gi 18621125 emb CAC87015.1 polymerase [Hepatitis B virus]	1471	0.0
gi 1359679 emb CAA66424.1 polymerase [Hepatitis B virus]	1470	0.0
gi 6692492 gb AAF24660.1 polymerase [Hepatitis B virus]	1468	0.0
gi 2182121 gb AAB59972.1 DNA polymerase [Hepatitis B virus]	1467	0.0
gi 4140295 emb CAA10539.1 polymerase [Hepatitis B virus]	1467	0.0
gi 28436096 dbj BAC57441.1 polymerase [Hepatitis B virus]	1466 1464	0.0
gi 2829156 gb AAC40810.1 polymerase [Hepatitis B virus] gi 27466519 gb AAO12604.1 polymerase [Hepatitis B virus] >.		0.0
gi 27466519 gb AAO12604.1 polymerase [Hepatitis B virus] >. gi 118869 sp P24024 DPOL_HPBVA P protein [Includes: DNA-dir.		0.0
	1461	0.0
gi 27466525 gb AAO12672.1 polymerase [Hepatitis B virus] gi 762933 emb CAA59514.1 polymerase [Hepatitis B virus]	1461	0.0
gi 22135690 gb AAM09033.1 polymerase [Hepatitis B virus]	1459	0.0
gi 6063470 dbj BAA85377.1 DNA polymerase/reverse transcrip.		0.0
gi 6063465 dbj BAA85373.1 DNA polymerase/reverse transcrip.		0.0
gi 27466605 gb AAO12660.1 polymerase [Hepatitis B virus]	1451	0.0
gi 2829149 gb AAC40804.1 polymerase [Hepatitis B virus]	1451	0.0
gi 475987 gb AAA18583.1 polymerase [Hepatitis B virus]	1450	0.0
gi 313784 emb CAA42466.1 polymerase [Hepatitis B virus]	1446	0.0
gi 27466597 gb AAO12653.1 polymerase [Hepatitis B virus]	1444	0.0
gi 15419833 gb AAK97182.1 AF297620_3 polymerase [Hepatitis .	1442	0.0
gi 93082 pir S20752 DNA-directed DNA polymerase (EC 2.7.7	1441	0.0
gi 27466613 gb AA012667.1 polymerase [Hepatitis B virus]	1435	0.0
gi 27466589 gb AAO12646.1 polymerase [Hepatitis B virus]	1434	0.0
gi 27466538 gb AAO12618.1 polymerase [Hepatitis B virus]	1432	0.0
gi 27466581 gb AA012639.1 polymerase [Hepatitis B virus]	1431	0.0
gi 15419828 gb AAK97178.1 AF297619_3 polymerase [Hepatitis .		0.0
gi 27466544 gb AA012681.1 polymerase [Hepatitis B virus]	1427	0.0
gi 27466557 gb AA012692.1 polymerase [Hepatitis B virus]	1423	0.0
gi 16751312 gb AAL25951.1 polymerase protein [Hepatitis B .		0.0
gi 11935073 gb AAG41955.1 AF305327_2 polymerase [Hepatitis .	1379	0.0
gi 13491150 gb AAK27856.1 AF330110_3 polymerase [Hepatitis .		0.0
gi 6116700 dbj BAA32859.2 pol protein [Hepatitis B virus]	1368	0.0
gi 3551332 dbj BAA32886.1 pol protein [Hepatitis B virus]	1368	0.0
gi 28812222 dbj BAC65108.1 polymerase protein [Hepatitis B. qi 6691505 dbj BAA89330.1 polymerase protein [Hepatitis B.		0.0 0.0
gi 6691505 dbj BAA89330.1 polymerase protein [Hepatitis B . gi 118872 sp P12900 DPOL_HPBVL P protein [Includes: DNA-dir.		0.0
gr 1100/2 Sp F12300 DFOD_REBVD F Process (includes: DNA-dir.	1506	0.0

```
gi | 560084 | dbj | BAA04927.1 |
                            DNA polymerase [Hepatitis B virus]
                                                                      1367
                                                                             0.0
gi|560089|dbj|BAA04931.1|
                            DNA polymerase [Hepatitis B virus]
                                                                      1367
                                                                             0.0
                                                                             0.0
qi | 6116731 | dbj | BAA32957.2 |
                             pol protein [Hepatitis B virus]
                                                                      1366
gi | 6691495 | dbj | BAA89322.1 |
                             polymerase protein [Hepatitis B ...
                                                                      1365
                                                                             0.0
qi|7188655|gb|AAF37833.1|AF222323 2 polymerase [Hepatitis B...
                                                                      1365
                                                                             0.0
                             DNA polymerase/reverse transcrip...
gi | 6063460 | dbj | BAA85369.1 |
                                                                             0.0
gi | 3551347 | dbj | BAA32898.1 |
                             pol protein [Hepatitis B virus]
                                                                             0.0
                             polymerase protein [Hepatitis B ...
gi | 6691500 | dbj | BAA89326.1 |
                                                                      1363
                                                                             0.0
gi | 28812217 | dbj | BAC65104.1 |
                                                                      1363
                                                                             0.0
                              polymerase protein [Hepatitis B...
gi|3551342|dbj|BAA32894.1|
                             pol protein [Hepatitis B virus]
                                                                      1363
                                                                             0.0
qi|628080|pir||S43491 DNA-directed DNA polymerase (EC 2.7.7...
                                                                      1363
                                                                             0.0
                                                                      1362
                                                                             0.0
qi|12246972|gb|AAG49670.1|AF223956 3 polymerase [Hepatitis ...
                                                                             0.0
                                                                      1362
gi|3551293|dbj|BAA32852.1| pol protein [Hepatitis B virus]
gi | 12246964 | gb | AAG49663.1 | AF223955_3 polymerase [Hepatitis ...
                                                                      1362
                                                                             0.0
                                                                             0.0
gi|21624231|dbj|BAC01103.1| polymerase protein [Hepatitis B...
                                                                      1362
                                                                             0.0
gi|118874|sp|P03157|DPOL_HPBVR P protein [Includes: DNA-dir...
                                                                      1361
qi|6009784|dbj|BAA85065.1| polymerase [Hepatitis B virus]
                                                                      1361
                                                                             0.0
gi|22651880|gb|AAN03491.1|AF286594_3
                                       DNA polymerase [Hepati...
                                                                      1360
                                                                             0.0
                                                                      1360
                                                                             0.0
gi|18252591|gb|AAL66348.1|AF461043_2
                                        P protein [Hepatitis B...
                                                                             0.0
gi|15778326|gb|AAL07381.1|AF411409_4 polymerase [Hepatitis ...
                                                                      1360
                             pol protein [Hepatitis B virus]
                                                                      1360
                                                                             0.0
gi|3551268|dbj|BAA32832.1|
gi|14290241|gb|AAK59316.1|AF384371_2 polymerase [Hepatitis ...
                                                                      1358
                                                                             0.0
                             DNA polymerase/reverse transcrip...
                                                                      1358
                                                                             0.0
gi | 6063435 | dbj | BAA85353.1 |
                                                                      1358
                                                                             0.0
gi | 6063440 | dbj | BAA85357.1 |
                             DNA polymerase/reverse transcrip...
                             pol protein [Hepatitis B virus]
                                                                      1358
                                                                             0.0
gi | 3551283 | dbj | BAA32844.1 |
gi|18252536|gb|AAL66307.1|AF458664_3 polymerase [Hepatitis ...
                                                                      1358
                                                                             0.0
                                                                      1358
                                                                             0.0
qi|6009769|dbj|BAA85053.1|
                             polymerase [Hepatitis B virus]
                                                                      1357
                                                                             0.0
gi|13991865|gb|AAK51533.1|AF363961_2 polymerase [Hepatitis ...
                                                                             0.0
qi | 6063425 | dbj | BAA85382.1 |
                             DNA polymerase/reverse transcrip...
                                                                      1357
                              DNA polymerase [Hepatitis B viru...
                                                                      1357
                                                                             0.0
qi | 2626986 | dbj | BAA23435.1 |
                              P protein [Hepatitis B virus]
                                                                      1357
                                                                             0.0
qi | 4490402 | emb | CAB38767.1 |
                             DNA polymerase/reverse transcrip...
                                                                      1357
                                                                             0.0
qi|22415735|gb|AAM95242.1|
gi|10934057|dbj|BAB16885.1| polymerase [Hepatitis B virus]
                                                                      1356
                                                                             0.0
qi|18252556|qb|AAL66323.1|AF461359 3 polymerase [Hepatitis ...
                                                                      1356
                                                                             0.0
                                                                             0.0
gi|2627009|dbj|BAA23455.1| DNA polymerase [Hepatitis B virus]
gi|560074|dbj|BAA04919.1| DNA polymerase [Hepatitis B virus]
                                                                      1356
                                                                             0.0
gi|479847|pir||S35527 DNA-directed DNA polymerase (EC 2.7.7...
                                                                             0.0
gi|18252545|gb|AAL66314.1|AF461357_2 polymerase [Hepatitis ...
                                                                      1356
                                                                             0.0
                              DNA polymerase [Hepatitis B virus]
                                                                      1355
                                                                             0.0
gi|1742906|dbj|BAA09083.1|
                                                                             0.0
gi | 6009764 | dbj | BAA85049.1 |
                              polymerase [Hepatitis B virus] >...
                                                                      1355
                              DNA polymerase [Hepatitis B virus]
                                                                      1355
                                                                             0.0
gi | 2627002 | dbj | BAA23449.1 |
                                                                             0.0
                              DNA polymerase/reverse transcrip...
                                                                      1355
gi | 6063455 | dbj | BAA85365.1 |
gi|10441115|gb|AAG16953.1|AF182804_4 polymerase [Hepatitis ...
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gi | 6009774 | dbj | BAA85057.1 |
                              polymerase [Hepatitis B virus]
                                                                      1353
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gi | 4490407 | emb | CAB38771.1 |
                              P protein [Hepatitis B virus]
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gi | 3582359 | dbj | BAA32913.1 |
                              pol protein [Hepatitis B virus]
                                                                      1353
                              pol protein [Hepatitis B virus]
                                                                      1353
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qi | 3582355 | dbj | BAA32874.1 |
gi|12246980|gb|AAG49677.1|AF223957_3 polymerase [Hepatitis
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                                                                             0.0
                              polymerase protein [Hepatitis B
                                                                      1352
                                                                             0.0
gi | 16751307 | gb | AAL25947.1 |
                              pol protein [Hepatitis B virus]
gi | 3582375 | dbj | BAA32925.1 |
                                                                      1352
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gi|15778340|gb|AAL07392.1|AF411412_4 polymerase [Hepatitis ...
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                                                                             0.0
gi|4206637|gb|AAD11755.1| DNA polymerase [Hepatitis B virus]
                                                                      1352
                                                                             0.0
gi|15425690|dbj|BAB64319.1| polymerase [Hepatitis B virus]
                                                                      1352
                                                                             0.0
                              pol protein [Hepatitis B virus]
gi | 3551352 | dbj | BAA32902.1 |
                                                                      1352
                                                                             0.0
                            pol protein [Hepatitis B virus]
                                                                      1352
                                                                             0.0
gi | 3582395 | dbj | BAA32963.1 |
gi|5114071|gb|AAD40205.1|AF090839_2 polymerase [Hepatitis B...
                                                                      1352
                                                                             0.0
gi|9082085|gb|AAF82723.1|AF233236_2 pol [Hepatitis B virus]
                                                                      1352
                                                                              0.0
gi|6983935|gb|AAF34734.1|AF160501_2 polymerase [Hepatitis B...
                                                                      1351
                                                                              0.0
gi|560094|dbj|BAA04935.1| DNA polymerase [Hepatitis B virus]
                                                                      1351
                                                                              0.0
gi|18032033|gb|AAL49990.1| polymerase [Hepatitis B virus]
                                                                      1351
                                                                              0.0
```

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1351
                                                                           0.0
gi|18146671|dbj|BAB82392.1| polymerase [Hepatitis B virus]
gi|6006322|dbj|BAA84819.1| polymerase protein [Hepatitis B ...
                                                                   1350
                                                                           0.0
gi|18252551|gb|AAL66319.1|AF461358_3 polymerase [Hepatitis ...
                                                                   1350
                                                                           0.0
gi|7188649|gb|AAF37828.1|AF222322_2 polymerase [Hepatitis B...
                                                                   1350
                                                                           0.0
                                                                           0.0
gi|12060441|dbj|BAB20611.1| DNA polymerase [Hepatitis B virus]
gi|18845085|gb|AAL79545.1|AF473543_4 P protein [Hepatitis B...
                                                                           0.0
gi|3551322|dbj|BAA32878.1| pol protein [Hepatitis B virus]
                                                                   1350
                                                                           0.0
                                                                   1350
                                                                           0.0
gi|12246956|gb|AAG49656.1|AF223954 4 polymerase [Hepatitis ...
                                                                           0.0
                                                                   1350
gi | 6063430 | dbj | BAA85349.1 |
                            DNA polymerase/reverse transcrip...
                            DNA polymerase [Hepatitis B virus]
                                                                   1350
                                                                           0.0
qi | 2288872 | dbj | BAA21665.1 |
gi|1220111|dbj|BAA04072.1|
                            DNA polymerase [Hepatitis B virus]
                                                                   1349
                                                                           0.0
                                                                           0.0
gi|9454168|gb|AAF87689.1|
                           polymerase protein [Hepatitis B v...
                                                                   1349
                                                                           0.0
qi|18146683|dbj|BAB82402.1| polymerase [Hepatitis B virus]
                                                                   1349
                            pol protein [Hepatitis B virus]
qi|3551278|dbj|BAA32840.1|
                                                                   1349
                                                                           0.0
                            pol protein [Hepatitis B virus]
                                                                   1349
                                                                           0.0
gi | 3551372 | dbj | BAA32939.1 |
gi|19849035|gb|AAL99437.1|AF405706_3 polymerase [Hepatitis
                                                                   1349
                                                                           0.0
                                                                           0.0
gi|3551357|dbj|BAA32906.1| pol protein [Hepatitis B virus]
                                                                   1349
gi|15778321|gb|AAL07377.1|AF411408_4 polymerase [Hepatitis ...
                                                                   1348
                                                                           0.0
gi|15072542|gb|AAK81690.1| polymerase protein [Hepatitis B ...
                                                                   1348
                                                                           0.0
gi|21624238|dbj|BAC01109.1| polymerase protein [Hepatitis B...
                                                                   1348
                                                                           0.0
                                                                           0.0
gi|12247012|gb|AAG49705.1|AF223961_3 polymerase [Hepatitis ...
                                                                   1348
                                                                           0.0
gi|5114086|gb|AAD40217.1|AF090842_2 polymerase [Hepatitis B...
                                                                   1348
                                                                   1347
                                                                           0.0
gi|3582407|dbj|BAA32972.1| pol protein [Hepatitis B virus]
                                                                           0.0
gi|15425698|dbj|BAB64325.1| polymerase [Hepatitis B virus]
                                                                   1347
                                                                   1347
                                                                           0.0
gi|18146665|dbj|BAB82387.1| polymerase [Hepatitis B virus]
gi|23194252|gb|AAN15074.1| P protein [Hepatitis B virus]
                                                                   1347
                                                                           0.0
                                                                           0.0
qi|560079|dbj|BAA04923.1| DNA polymerase [Hepatitis B virus]
                                                                   1347
gi|10443833|gb|AAG17595.1|AF241410_3 polymerase [Hepatitis ...
                                                                   1346
                                                                           0.0
gi|13991870|gb|AAK51537.1|AF363962_2 polymerase [Hepatitis ...
                                                                   1346
                                                                           0.0
                                                                           0.0
gi | 4007054 | emb | CAA10426.1 |
                            DNA polymerase [Hepatitis B virus]
                                                                   1346
gi|3551362|dbj|BAA32910.1| pol protein [Hepatitis B virus]
                                                                           0.0
gi|18146677|dbj|BAB82397.1| polymerase [Hepatitis B virus]
                                                                           0.0
gi|12246988|gb|AAG49684.1|AF223958_3 polymerase [Hepatitis
                                                                   1346
                                                                           0.0
gi|15211897|emb|CAC51286.1| polymerase [Hepatitis B virus]
                                                                   1345
                                                                           0.0
gi|18389989|gb|AAL68823.1| polymerase [Hepatitis B virus]
                                                                   1345
                                                                           0.0
                                                                   1345
                                                                           0.0
                            pol protein [Hepatitis B virus]
gi | 3582363 | dbj | BAA32916.1 |
gi|10441110|gb|AAG16949.1|AF182803_4 polymerase [Hepatitis
                                                                           0.0
                                                                   1345
gi | 10443841 | gb | AAG17602.1 | AF241411_3 polymerase [Hepatitis
                                                                   1345
                                                                           0.0
                            pol protein [Hepatitis B virus]
                                                                   1345
                                                                           0.0
gi | 3551382 | dbj | BAA32947.1 |
                            pol protein [Hepatitis B virus]
                                                                   1344
                                                                           0.0
gi|3582387|dbj|BAA32950.1|
                            pol protein [Hepatitis B virus]
gi | 3551317 | dbj | BAA32871.1 |
                                                                   1344
                                                                           0.0
gi|10441104|gb|AAG16944.1|AF182802_3 polymerase [Hepatitis ...
                                                                   1343
                                                                           0.0
gi|118866|sp|P03159|DPOL_HPBV2 P protein [Includes: DNA-dir...
                                                                   1343
                                                                           0.0
gi|15425694|dbj|BAB64322.1| polymerase [Hepatitis B virus]
                                                                   1343
                                                                           0.0
                            DNA polymerase [Hepatitis B virus]
                                                                   1343
                                                                           0.0
gi | 4007049 | emb | CAA10422.1 |
                             pol protein [Hepatitis B virus]
gi|29123239|gb|AA062971.1|
                                                                   1343
                                                                           0.0
gi|4007064|emb|CAA10438.1| DNA polymerase [Hepatitis B virus]
                                                                   1342
                                                                           0.0
                           polymerase [Hepatitis B virus]
gi | 452623 | emb | CAA53358.1 |
                                                                    1342
                                                                           0.0
gi|18252541|gb|AAL66311.1|AF458665_3 polymerase [Hepatitis ...
                                                                    1342
                                                                           0.0
gi|527443|emb|CAA84791.1| DNA polymerase [Hepatitis B virus]
                                                                   1342
                                                                           0.0
                              polymerase [Hepatitis B virus]
                                                                    1342
                                                                           0.0
gi | 15211890 | emb | CAC51280.1 |
                                                                    1341
                                                                           0.0
gi|329617|gb|AAA62812.1| DNA polymerase
gi|4007079|emb|CAA10454.1| DNA polymerase [Hepatitis B virus]
                                                                    1341
                                                                           0.0
                           polymerase protein [Hepatitis B v...
                                                                    1341
                                                                           0.0
gi|9454173|gb|AAF87693.1|
gi|452628|emb|CAA53354.1| polymerase [Hepatitis B virus]
                                                                    1341
                                                                           0.0
gi|3582367|dbj|BAA32919.1| pol protein [Hepatitis B virus]
                                                                    1340
                                                                           0.0
gi|5114066|gb|AAD40201.1|AF090838_2 polymerase [Hepatitis B...
                                                                   1340
                                                                           0.0
gi|15419860|gb|AAK97203.1|AF297625_3 polymerase [Hepatitis ...
                                                                   1340
                                                                           0.0
                                                                   1340
gi|4490412|emb|CAB38775.1| P protein [Hepatitis B virus]
                                                                           0.0
gi|18252566|gb|AAL66331.1|AF461361_3 polymerase [Hepatitis ...
                                                                   1340
                                                                           0.0
```

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qi|4007059|emb|CAA10430.1| DNA polymerase [Hepatitis B virus]
                                                                      1340
                                                                              0.0
qi|5114081|qb|AAD40213.1|AF090841 2 polymerase [Hepatitis B...
                                                                      1339
                                                                              0.0
                              pol protein [Hepatitis B virus]
qi | 3582371 | dbj | BAA32922.1 |
                                                                      1339
                                                                              0.0
gi|12247003|gb|AAG49697.1|AF223960_4 polymerase [Hepatitis ...
                                                                      1339
                                                                              0.0
gi | 4033548 | emb | CAA10450.1 |
                              DNA polymerase [Hepatitis B virus]
                                                                      1339
                                                                              0.0
                              polymerase [Hepatitis B virus]
                                                                      1339
                                                                              0.0
gi | 3892581 | emb | CAA09962.1 |
gi|5114076|gb|AAD40209.1|AF090840_2 polymerase [Hepatitis B...
                                                                      1338
                                                                              0.0
                                                                              0.0
gi|12060436|dbj|BAB20607.1| DNA polymerase [Hepatitis B virus]
                                                                      1338
gi|118868|sp|P17100|DPOL_HPBV9 P protein [Includes: DNA-dir...
                                                                      1337
                                                                              0.0
                              polymerase [Hepatitis B virus]
                                                                              0.0
                                                                      1337
gi | 27466434 | gb | AAO12555.1 |
gi | 3582399 | dbj | BAA32966.1 |
                                                                      1337
                              pol protein [Hepatitis B virus]
                                                                              0.0
gi | 3551273 | dbj | BAA32836.1 |
                              pol protein [Hepatitis B virus]
                                                                      1337
                                                                              0.0
qi | 14285168 | qb | AAK58873.1 |
                              polymerase [synthetic construct]...
                                                                      1337
                                                                              0.0
gi | 3582391 | dbj | BAA32953.1 |
                              pol protein [Hepatitis B virus]
                                                                      1337
                                                                              0.0
gi|15419845|gb|AAK97191.1|AF297622_3 polymerase [Hepatitis ...
                                                                      1337
                                                                              0.0
gi|118870|sp|P17393|DPOL HPBVI P protein [Includes: DNA-dir...
                                                                      1336
                                                                              0.0
gi | 3551377 | dbj | BAA32943.1 |
                             pol protein [Hepatitis B virus]
                                                                      1336
                                                                              0.0
gi|10443825|gb|AAG17588.1|AF241409_3 polymerase [Hepatitis ...
                                                                      1336
                                                                              0.0
gi|10443817|gb|AAG17581.1|AF241408_3 polymerase [Hepatitis ...
                                                                      1336
                                                                              0.0
                                                                              0.0
gi | 29124889 | gb | AAO63519.1 |
                              pol protein [Hepatitis B virus]
                                                                      1335
gi|399401|sp|P31870|DPOL_HPBVM P protein [Includes: DNA-dir...
                                                                      1335
                                                                              0.0
                                                                              0.0
gi | 6063445 | dbj | BAA85339.1 |
                             DNA polymerase/reverse transcrip...
                                                                      1335
gi|19568078|gb|AAL89566.1|
                              polymerase [Hepatitis B virus]
                                                                      1334
                                                                              0.0
                                                                              0.0
gi | 27466426 | gb | AAO12548.1 |
                              polymerase [Hepatitis B virus]
                                                                      1334
gi|22655601|gb|AAN04128.1| polymerase [Hepatitis B virus]
                                                                      1334
                                                                              0.0
qi|8161369|qb|AAA69721.2| polymerase [Hepatitis B virus]
                                                                      1334
                                                                              0.0
gi|10441120|gb|AAG16957.1|AF182805_4 polymerase [Hepatitis ...
                                                                      1334
                                                                              0.0
qi|10443809|gb|AAG17574.1|AF241407_3 polymerase [Hepatitis
                                                                              0.0
gi|18146689|dbj|BAB82407.1| polymerase [Hepatitis B virus]
                                                                      1333
                                                                              0.0
gi | 4007069 | emb | CAA10442.1 |
                              DNA polymerase [Hepatitis B virus]
                                                                      1333
                                                                              0.0
gi|18031709|gb|AAK57744.1|
                              polymerase [Hepatitis B virus]
                                                                      1333
                                                                              0.0
gi|18252561|gb|AAL66327.1|AF461360_3 polymerase [Hepatitis ...
                                                                      1332
                                                                              0.0
\verb|gi|6959503|gb|AAF33121.1| & polymerase protein [orangutan hep...
                                                                      1332
                                                                              0.0
gi | 26224721 | gb | AAN76318.1 |
                              polymerase [Hepatitis B virus]
                                                                      1332
                                                                              0.0
gi | 4007074 | emb | CAA10446.1 |
                              DNA polymerase [Hepatitis B virus]
                                                                      1332
                                                                              0.0
gi | 18031714 | gb | AAK57745.1 |
                              polymerase [Hepatitis B virus]
                                                                      1332
                                                                              0.0
gi|7434791|pir||S67505 DNA-directed DNA polymerase (EC 2.7....
                                                                      1332
                                                                              0.0
gi|15419855|gb|AAK97199.1|AF297624 3 polymerase [Hepatitis ...
                                                                      1332
                                                                              0.0
gi|7434793|pir||T13468 DNA-directed DNA polymerase (EC 2.7....
                                                                      1331
                                                                              0.0
gi | 4323205 | gb | AAD16257.1 | polymerase [Hepatitis B virus]
                                                                      1331
                                                                              0.0
gi|12060194|dbj|BAB20451.1| DNA polymerase [Hepatitis B virus]
                                                                      1331
                                                                              0.0
gi | 23194347 | gb | AAN15122.1 |
                              polymerase [Hepatitis B virus]
                                                                      1330
                                                                              0.0
gi | 20151228 | gb | AAM12945.1 |
                              DNA polymerase/reverse transcrip...
                                                                      1330
                                                                              0.0
gi | 23884547 | gb | AAN40009.1 |
                              pol protein [Hepatitis B virus]
                                                                      1330
                                                                              0.0
gi|21431681|gb|AAM53414.1|U87747_3 DNA polymerase/reverse t...
                                                                      1330
                                                                              0.0
gi|3551337|dbj|BAA32890.1| pol protein [Hepatitis B virus]
                                                                      1329
                                                                              0.0
gi | 5019933 | gb | AAD37919.1 |
                            P protein [Hepatitis B virus]
                                                                      1329
                                                                              0.0
gi|15419840|gb|AAK97187.1|AF297621_3 polymerase [Hepatitis ...
                                                                      1329
                                                                              0.0
gi | 6006331 | dbj | BAA84825.1 |
                              polymerase protein [Hepatitis B
                                                                      1329
                                                                              0.0
                                                                              0.0
gi | 19568073 | gb | AAL89569.1 |
                              polymerase [Hepatitis B virus]
                                                                      1329
                                                                      1328
gi|29124918|gb|AAO63539.1| pol protein [Hepatitis B virus]
                                                                              0.0
gi 329630 gb AAA45483.1 P protein [Hepatitis B virus]
                                                                      1328
                                                                              0.0
gi|15778331|gb|AAL07385.1|AF411410_4 polymerase [Hepatitis ...
                                                                      1328
                                                                              0.0
                                                                      1328
gi | 6566410 | dbj | BAA88275.1 |
                              P protein [Hepatitis B virus]
                                                                              0.0
                                                                      1328
qi | 4490397 | emb | CAB38763.1 |
                              P protein [Hepatitis B virus]
                                                                              0.0
gi | 12060187 | dbj | BAB20445.1 |
                              DNA polymerase [Hepatitis B virus]
                                                                      1327
                                                                              0.0
gi | 6063450 | dbj | BAA85343.1 |
                              DNA polymerase/reverse transcrip...
                                                                      1327
                                                                              0.0
gi|118877|sp|P03155|DPOL_HPBVZ P protein [Includes: DNA-dir...
                                                                      1327
                                                                              0.0
gi | 29124883 | gb | AAO63514.1 |
                              pol protein [Hepatitis B virus]
                                                                      1325
                                                                              0.0
gi | 4033543 | emb | CAA10434.1 |
                              DNA polymerase [Hepatitis B virus]
                                                                      1325
                                                                              0.0
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gi | 6692525 | gb | AAF24693.1 |
                              polymerase [Hepatitis B virus]
                                                                        1325
                                                                                0.0
qi | 6692559 | gb | AAF24727.1 |
                              polymerase [Hepatitis B virus]
                                                                        1325
                                                                                0.0
gi | 23194340 | gb | AAN15116.1 |
                               polymerase [Hepatitis B virus]
                                                                        1325
                                                                                0.0
                              DNA polymerase [Hepatitis B virus]
gi | 560064 | dbj | BAA04911.1 |
                                                                        1324
                                                                                0.0
gi | 29124898 | gb | AA063526.1 |
                               pol protein [Hepatitis B virus]
                                                                        1324
                                                                                0.0
                               pol protein [Hepatitis B virus]
gi | 29124927 | gb | AA063545.1 |
                                                                        1323
                                                                                0.0
                              polymerase [Hepatitis B virus]
                                                                        1323
                                                                                0.0
gi | 6692566 | gb | AAF24734.1 |
                              polymerase [Hepatitis B virus]
                                                                        1323
                                                                                0.0
gi | 6692553 | gb | AAF24721.1 |
                              polymerase [Hepatitis B virus] >g...
                                                                                0.0
                                                                        1323
gi | 6692518 | gb | AAF24686.1 |
                               polymerase [Hepatitis B virus] >...
                                                                                0.0
gi | 1359702 emb | CAA66444.1 |
                                                                        1323
                                                                                0.0
                               pol protein [Hepatitis B virus]
                                                                        1323
gi | 29124867 | gb | AA063501.1 |
gi | 29124872 | gb | AA063505.1 |
                               pol protein [Hepatitis B virus]
                                                                        1323
                                                                                0.0
qi | 27466479 | qb | AA012576.1 |
                               polymerase [Hepatitis B virus]
                                                                        1322
                                                                                0.0
gi | 6692546 | gb | AAF24714.1 |
                             polymerase [Hepatitis B virus]
                                                                        1322
                                                                                0.0
                              pol protein [Hepatitis B virus]
                                                                        1322
                                                                                0.0
gi | 3551312 | dbj | BAA32867.1 |
gi | 27466487 | gb | AAO12611.1 |
                               polymerase [Hepatitis B virus]
                                                                        1322
                                                                                0.0
                                                                        1321
gi|118871|sp|P17394|DPOL_HPBVJ P protein [Includes: DNA-dir...
                                                                                0.0
gi|9454473|gb|AAF87833.1|AF282917_3 DNA polymerse [Hepatiti...
                                                                        1321
                                                                                0.0
gi|19224214|gb|AAL86445.1|AF479684_3 P gene product [Hepati...
                                                                        1321
                                                                                0.0
                             polymerase [Hepatitis B virus]
                                                                        1321
                                                                                0.0
gi | 6692572 | gb | AAF24740.1 |
                                                                        1321
                                                                                0.0
gi | 3551297 | dbj | BAA32855.1 |
                              pol protein [Hepatitis B virus]
                                                                        1320
                                                                                0.0
gi | 3551327 | dbj | BAA32882.1 |
                               pol protein [Hepatitis B virus]
                               polymerase [Hepatitis B virus]
                                                                        1320
                                                                                0.0
gi | 1359695 | emb | CAA66434.1 |
                               pol protein [Hepatitis B virus]
                                                                        1320
                                                                                0.0
gi | 3551367 | dbj | BAA32932.1 |
                                                                        1319
                                                                                0.0
gi|118873|sp|P17395|DPOL_HPBVO P protein [Includes: DNA-dir...
gi | 29124862 | gb | AAO63497.1 |
                               pol protein [Hepatitis B virus]
                                                                        1319
                                                                                0.0
gi | 18621110 | emb | CAC87028.1 |
                                polymerase [Hepatitis B virus]
                                                                        1319
                                                                                0.0
qi|3582403|dbj|BAA32969.1|
                               pol protein [Hepatitis B virus]
                                                                        1318
                                                                                0.0
                               DNA polymerase [Hepatitis B viru...
                                                                        1318
                                                                                0.0
gi | 27261550 | gb | AAN85925.1 |
gi | 1914703 | emb | CAA66699.1 |
                                                                        1318
                                                                                0.0
                               polymerase [Hepatitis B virus]
gi | 4323200 | gb | AAD16253.1 |
                             polymerase [Hepatitis B virus]
                                                                        1318
                                                                                0.0
qi | 6573293 | dbj | BAA88291.1 |
                               P protein [Hepatitis B virus]
                                                                        1318
                                                                                0.0
gi | 6006341 | dbj | BAA84833.1 |
                               polymerase protein [Hepatitis B ...
                                                                        1316
                                                                                0.0
                               P protein [Hepatitis B virus]
gi | 6566440 | dbj | BAA88286.1 |
                                                                        1315
                                                                                0.0
                             DNA polymerase [Hepatitis B virus]
                                                                        1315
                                                                                0.0
gi|560059|dbj|BAA04907.1|
                              polymerase [Hepatitis B virus]
                                                                        1315
                                                                                0.0
gi | 14334410 | gb | AAK59391.1 |
                             P protein [Hepatitis B virus]
                                                                        1315
                                                                                0.0
gi | 5019954 | gb | AAD37936.1 |
gi|16117323|dbj|BAB69785.1| polymerase [Hepatitis B virus]
                                                                        1315
                                                                                0.0
gi|7434792|pir||T13473 DNA-directed DNA polymerase (EC 2.7....
                                                                                0.0
                                                                        1315
                             P protein [Hepatitis B virus]
gi | 5019965 | gb | AAD37945.1 |
                                                                        1314
                                                                                0.0
                                                                        1314
gi | 29124908 | gb | AA063533.1 |
                              pol protein [Hepatitis B virus]
                                                                                0.0
                                                                        1313
gi | 6566428 | dbj | BAA88281.1 |
                               P protein [Hepatitis B virus]
                                                                                0.0
                               pol protein [Hepatitis B virus]
gi | 29124894 | gb | AA063523.1 |
                                                                        1311
                                                                                0.0
gi | 22135730 | gb | AAM09065.1 |
                              polymerase [Hepatitis B virus]
                                                                        1311
                                                                                0.0
                             DNA polymerase [Hepatitis B virus]
                                                                        1311
                                                                                0.0
gi | 560069 | dbj | BAA04915.1 |
gi|15419850|gb|AAK97195.1|AF297623_3 polymerase [Hepatitis ...
                                                                        1311
                                                                                0.0
                                polymerase protein [orangutan h...
gi | 9634217 | ref | NP_037757.1 |
                                                                        1310
                                                                                0.0
gi | 16117333 | dbj | BAB69793.1 |
                                polymerase [Hepatitis B virus]
                                                                        1309
                                                                                0.0
gi | 9971630 | dbj | BAB12582.1 |
                               polymerase protein [Hepatitis B
                                                                        1308
                                                                                0.0
                               polymerase [Hepatitis B virus]
                                                                        1306
                                                                                0.0
gi | 27466450 | gb | AAO12569.1 |
gi|12247036|gb|AAG49726.1|AF223964_3 polymerase [Hepatitis
                                                                        1306
                                                                                0.0
gi|12247028|gb|AAG49719.1|AF223963_3 polymerase [Hepatitis
                                                                        1305
                                                                                0.0
gi|5019945|gb|AAD37929.1| P protein [Hepatitis B virus]
                                                                        1305
                                                                                0.0
gi|18146701|dbj|BAB82417.1| polymerase [Hepatitis B virus]
                                                                        1305
                                                                                0.0
gi|12247020|gb|AAG49712.1|AF223962_3 polymerase [Hepatitis
                                                                        1304
                                                                                0.0
gi|5019981|gb|AAD37958.1| P protein [Hepatitis B virus]
                                                                        1304
                                                                                0.0
                                                                        1304
                                                                                0.0
gi|3892582|emb|CAA53343.1| polymerase [Hepatitis B virus]
                               polymerase [Hepatitis B virus]
                                                                        1304
                                                                                0.0
gi | 27466442 | gb | AAO12562.1 |
gi|22135715|gb|AAM09053.1| polymerase [Hepatitis B virus]
                                                                        1301
                                                                                0.0
gi|12247044|gb|AAG49733.1|AF223965_3 polymerase [Hepatitis ...
                                                                        1301
                                                                                0.0
```

```
polymerase [Hepatitis B virus]
                                                                       1301
                                                                               0.0
gi | 22135725 | gb | AAM09061.1 |
                               polymerase [Hepatitis B virus]
                                                                       1300
                                                                               0.0
gi | 11191880 | dbj | BAB17962.1 |
                              pol protein [Hepatitis B virus]
                                                                       1300
                                                                               0.0
gi | 3551392 | dbj | BAA32961.1 |
                                                                       1299
                                                                               0.0
qi | 6006336 | dbj | BAA84829.1 |
                              polymerase protein [Hepatitis B ...
                                                                       1298
                                                                               0.0
gi | 2627021 | dbj | BAA23467.1 |
                              DNA polymerase [Hepatitis B virus]
                                                                       1297
                              DNA polymerase [Hepatitis B virus]
                                                                               0.0
qi | 2627015 | dbj | BAA23461.1 |
gi | 16117328 | dbj | BAB69789.1 |
                               polymerase [Hepatitis B virus]
                                                                       1297
                                                                               0.0
                              polymerase [Hepatitis B virus]
                                                                       1297
                                                                               0.0
gi | 22135735 | gb | AAM09069.1 |
gi|14485226|gb|AAK62976.1|AF384372_2 polymerase [Hepatitis ...
                                                                       1296
                              pol protein [Hepatitis B virus]
gi | 3551288 | dbj | BAA32848.1 |
                                                                       1295
                                                                               0.0
                               polymerase [Hepatitis B virus]
                                                                       1294
                                                                               0.0
qi|11191960|dbj|BAB18032.1
                               polymerase [Hepatitis B virus]
                                                                       1293
                                                                               0.0
qi | 11191888 | dbj | BAB17969.1
gi|11191840|dbj|BAB17927.1
                               polymerase [Hepatitis B virus]
                                                                       1293
                                                                               0.0
                               polymerase [Hepatitis B virus]
gi|11191920|dbj|BAB17997.1
                                                                       1293
                                                                               0.0
                               polymerase [Hepatitis B virus]
                                                                               0.0
gi|11191904|dbj|BAB17983.1
                                                                       1291
                               polymerase [Hepatitis B virus]
gi | 11191952 | dbj | BAB18025.1 |
                                                                       1291
                                                                               0.0
gi|1169410|sp|Q05486|DPOL_HPBVT P protein [Includes: DNA-di...
                                                                       1289
                                                                               0.0
gi | 22135705 | gb | AAM09045.1 |
                              polymerase [Hepatitis B virus]
                                                                       1288
                                                                               0.0
gi | 452633 | emb | CAA53350.1 |
                             polymerase [Hepatitis B virus]
                                                                       1288
                                                                               0.0
                               polymerase [Hepatitis B virus]
                                                                       1287
gi | 18146695 | dbj | BAB82412.1 |
                                                                               0.0
gi|22135710|gb|AAM09049.1|
                              polymerase [Hepatitis B virus]
                                                                       1287
                                                                               0.0
                               polymerase [Hepatitis B virus]
                                                                       1286
                                                                               0.0
gi | 11191864 | dbj | BAB17948.1 |
gi|59451|emb|CAA48354.1| HBV polymerase [Hepatitis B virus]
                                                                       1286
                                                                               0.0
                                                                       1286
                                                                               0.0
gi | 11191848 | dbj | BAB17934.1 |
                               polymerase [Hepatitis B virus] ...
gi|22135700|gb|AAM09041.1|
                              polymerase [Hepatitis B virus]
                                                                       1285
                                                                               0.0
gi|5019976|gb|AAD37954.1|
                             P protein [Hepatitis B virus]
                                                                       1281
                                                                               0.0
                             polymerase [Hepatitis B virus]
gi | 22135720 | gb | AAM09057.1 |
                                                                       1279
                                                                               0.0
                                                                       1276
                                                                               0.0
gi | 5019939 | gb | AAD37924.1 |
                             P protein [Hepatitis B virus]
                                                                               0.0
gi | 1914697 | emb | CAA66674.1 |
                              polymerase [Hepatitis B virus]
                                                                       1273
                              polymerase [Hepatitis B virus]
                                                                       1271
                                                                               0.0
qi | 1914691 | emb | CAA66679.1 |
                             P protein [Hepatitis B virus]
                                                                       1263
                                                                               0.0
gi|5019970|gb|AAD37949.1|
                                                                       1258
                                                                               0.0
qi|15425702|dbj|BAB64328.1| polymerase [Hepatitis B virus]
gi|29124905|gb|AA063531.1|
                              pol protein [Hepatitis B virus]
                                                                       1253
                                                                               0.0
                              polymerase [Hepatitis B virus]
gi | 27466464 | gb | AAO12704.1 |
                                                                       1248
                                                                               0.0
                              polymerase [Hepatitis B virus]
gi|27466471|gb|AA012710.1|
                                                                       1244
                                                                               0.0
                                                                       1243
                                                                               0.0
gi|18252571|gb|AAL66335.1|AF461362_3 polymerase [Hepatitis
                              polymerase [Hepatitis B virus]
                                                                       1239
                                                                               0.0
gi | 27466511 | gb | AAO12597.1 |
gi|27466457|gb|AA012698.1|
                              polymerase [Hepatitis B virus]
                                                                       1238
                                                                               0.0
                                                                       1227
                                                                               0.0
gi | 15211905 | emb | CAC51293.1 |
                               polymerase [Hepatitis B virus]
gi|399402|sp|Q02314|DPOL_HPBVP P protein {Includes: DNA-dir...
                                                                       1224
                                                                               0.0
gi | 1914708 | emb | CAA66684.1 |
                              polymerase [Hepatitis B virus]
                                                                       1220
                                                                               0.0
                                                                       1184
                                                                               0.0
gi | 27466503 | gb | AAO12583.1 |
                              polymerase [Hepatitis B virus]
gi|118867|sp|P12933|DPOL_HPBV4 P protein [Includes: DNA-dir...
                                                                       1157
                                                                               0.0
gi | 4468850 | emb | CAB38229.1 |
                              polymerase [Hepatitis B virus]
                                                                       1122
                                                                               0.0
                              polymerase [Hepatitis B virus]
                                                                       1101
                                                                               0.0
gi | 1914719 | emb | CAA66694.1 |
                              polymerase [woolly monkey hepat...
gi | 9630375 | ref | NP_046799.1 |
                                                                       1049
                                                                               0.0
gi | 1185115 | emb | CAA51254.1 |
                              DNA polymerase [Hepatitis B virus]
                                                                        922
                                                                               0.0
gi|20800461|gb|AAM28642.1|U87746_4 DNA polymerase/reverse t...
                                                                        910
                                                                               0.0
                               P gene product (AA 304-843); c...
gi | 21326585 | ref | NP_647604.1 |
                                                                        907
                                                                               0.0
                                                                        904
                                                                               0.0
gi | 4377612 | emb | CAA53339.1 |
                              polymerase [Hepatitis B virus]
                              polymerase [Hepatitis B virus]
                                                                        901
                                                                               0.0
gi | 4377613 | emb | CAA53338.1 |
                                                                        898
                                                                               0.0
gi | 1549226 | dbj | BAA04073.1 |
                              ORF [Hepatitis B virus]
                                                                        895
gi|9454414|gb|AAF87797.1| polymerase [Hepatitis B virus]
                                                                               0.0
                                                                        893
                                                                               0.0
                              ORF [Hepatitis B virus]
gi|1550614|dbj|BAA04075.1|
                                                                        879
gi|59409|emb|CAA32399.1| DNA polymerase [Hepatitis B virus]
                                                                               0.0
                                                                        727
gi|118894|sp|P03160|DPOL_WHV1 P protein [Includes: DNA-dire...
                                                                               0.0
gi|9626716|ref|NP_040994.1| A protein [Ground squirrel hepa...
                                                                        727
                                                                               0.0
                                                                        725
gi|22256032|ref|NP 671813.1| DNA polymerase [Woodchuck hepa...
                                                                               0.0
gi|15637595|gb|AAL04547.1|AF410859_1 polymerase [Woodchuck ...
                                                                        725
                                                                               0.0
gi|15637587|gb|AAL04543.1|AF410855_1 type II mutant polymer...
                                                                        725
                                                                               0.0
```

```
724
                                                                             0.0
gi|118895|sp|P12899|DPOL WHV59 P protein [Includes: DNA-dir...
qi|15637597|gb|AAL04548.1|AF410860 1 polymerase [Woodchuck ...
                                                                       724
                                                                             0.0
                                                                       722
                                                                             0.0
qi | 15637599 | qb | AAL04549.1 | AF410861 1
                                       polymerase [Woodchuck ...
qi|15637593|gb|AAL04546.1|AF410858 1 defective polymerase [...
                                                                       721
                                                                             0.0
gi|118898|sp|P17396|DPOL_WHV8I P protein [Includes: DNA-dir...
                                                                       721
                                                                             0.0
                                        type I mutant polymera...
                                                                       721
                                                                             0.0
gi|15637591|gb|AAL04545.1|AF410857_1
qi|15637589|gb|AAL04544.1|AF410856 1 type IV mutant polymer...
                                                                       717
                                                                             0.0
                                                                       706
gi|118897|sp|P06275|DPOL_WHV8 P protein [Includes: DNA-dire...
                                                                             0.0
qi|3582379|dbj|BAA32928.1| pol protein [Hepatitis B virus]
                                                                       692
                                                                             0.0
gi|9885813|gb|AAG01539.1|AF291830_2 polymerase [Hepatitis B...
                                                                       692
                                                                             0.0
gi | 118875 | sp | P03158 | DPOL_HPBVW DNA polymerase
                                                                       680
                                                                             0.0
gi|9628830|ref|NP_043864.1| polymerase [Arctic ground squir...
                                                                       669
                                                                             0.0
                                                                       669
                                                                             0.0
qi | 8926931 | dbj | BAA98025.1 |
                             pol protein [Hepatitis B virus]
                                                                       667
                                                                             0.0
qi | 8926928 | dbj | BAA98023.1 |
                             pol protein [Hepatitis B virus]
                             pol protein [Hepatitis B virus]
                                                                       667
gi | 8926925 | dbj | BAA98021.1 |
                                                                             0.0
                             pol protein [Hepatitis B virus]
                                                                       655
qi | 8926934 | dbj | BAA98027.1 |
                                                                             0.0
gi | 13345982 | gb | AAK19538.1 | AF335734_2
                                        polymerase [Hepatitis ...
                                                                       583
                                                                            e-166
gi | 12083172 | gb | AAG48743.1 | AF329861_2
                                        polymerase [Hepatitis ...
                                                                       583
                                                                            e-166
                                                                       583
                                                                            e-166
gi|13345979|gb|AAK19536.1|AF335733_2
                                        polymerase
                                                    [Hepatitis ...
                                        polymerase [Hepatitis ...
                                                                       582
gi | 12083181 | gb | AAG48749.1 | AF329864_2
                                                                            e-166
                                        polymerase [Hepatitis ...
gi | 12083178 | gb | AAG48747.1 | AF329863_2
                                                                       582
                                                                            e-165
                                        polymerase [Hepatitis ...
                                                                       581
                                                                            e-165
gi|12083163|gb|AAG48737.1|AF329858_1
                                        polymerase [Hepatitis ...
gi | 12083167 | gb | AAG48740.1 | AF329859_2
                                                                       581
                                                                            e-165
                                                                       580
                                                                            e-165
gi|13345988|gb|AAK19542.1|AF335736_2
                                        polymerase [Hepatitis ...
gi|13345985|gb|AAK19540.1|AF335735_2 polymerase [Hepatitis ...
                                                                       578
                                                                            e-164
gi|2982339|gb|AAC06361.1| DNA polymerase [Hepatitis B virus]
                                                                       568
                                                                            e-161
                                                                       566
                                                                            e-161
gi|336159|gb|AAA46774.1| polymerase protein
gi|118899|sp|P11292|DPOL_WHVW6 P protein [Includes: DNA-dir...
                                                                       560
                                                                            e-159
                                                                       555
gi|225532|prf||1305266C gene P
                                                                            e-157
                                                                       540
gi | 1107586 | emb | CAA56892.1 |
                              polymerase [Hepatitis B virus]
                                                                            e-153
                              polymerase [Hepatitis B virus]
                                                                       538
                                                                            e-152
qi | 1107579 | emb | CAA56878.1 |
                                                                       465
                                                                            e-130
gi|1185116|emb|CAA51255.1| HBsAg [Hepatitis B virus]
gi|59414|emb|CAA32405.1| DNA polymerase [Hepatitis B virus]
                                                                       459
                                                                            e-129
gi|21326589|ref|NP_647608.1| P gene product, put.DNA polyme...
                                                                       458
                                                                            e-128
gi|1321828|emb|CAA96556.1| polymerase [Hepatitis B virus]
                                                                       441
                                                                            e-123
gi|5019960|gb|AAD37941.1| P protein [Hepatitis B virus]
                                                                       440
                                                                            e-123
                                                                       433
                                                                            e-121
                           coat protein [Hepatitis B virus]
gi|329652|gb|AAA69719.1|
                                                                       429
                                                                            e-120
                           coat protein [Hepatitis B virus]
gi|329651|gb|AAA69720.1|
gi|27466495|gb|AA012590.1| polymerase [Hepatitis B virus]
                                                                       429
                                                                            e - 120
                                                                       413
gi|21218028|dbj|BAB96528.1| large S protein [Hepatitis B vi...
                                                                            e-115
                                                                       410
                                                                            e-114
gi|1321832|emb|CAA96561.1| polymerase [Hepatitis B virus]
gi|27450190|gb|AA014552.1|AF460225_1 polymerase [Hepatitis
                                                                       385
                                                                            e - 106
gi 27450188 gb AA014551.1 AF460224_1
                                        polymerase [Hepatitis
                                                                       384
                                                                            e-106
gi|27450192|gb|AA014553.1|AF460226_1
                                        polymerase [Hepatitis
                                                                       383
                                                                            e-106
gi|27450198|gb|AA014556.1|AF460229_1
                                        polymerase [Hepatitis
                                                                       382
                                                                            e-105
gi|27450196|gb|AA014555.1|AF460228_1
                                        polymerase [Hepatitis
                                                                       382
                                                                            e-105
gi|27450194|gb|AA014554.1|AF460227_1
                                        polymerase [Hepatitis ...
                                                                       382
                                                                            e-105
                                        polymerase [Hepatitis ...
gi | 27450200 | gb | AA014557.1 | AF460230_1
                                                                       375
                                                                            e-103
                                                                       375
                                                                            e-103
gi|27450202|gb|AA014558.1|AF460231_1 polymerase [Hepatitis ...
                                                                       374
                            DNA polymerase [Hepatitis B virus]
                                                                            e-103
gi | 3328370 | gb | AAC26832.1 |
                                                                       373
                              polymerase [Hepatitis B virus]
                                                                            e - 103
gi | 23380174 | gb | AAM83022.1 |
                              polymerase [Hepatitis B virus]
                                                                       373
                                                                            e-103
gi|23380081|gb|AAM82960.1|
                              polymerase [Hepatitis B virus]
                                                                       372
                                                                            e-102
gi|23380171|gb|AAM83020.1
                              polymerase [Hepatitis B virus]
                                                                       370
                                                                            e-102
gi|23380180|gb|AAM83026.1
                              polymerase [Hepatitis B virus]
                                                                       369
                                                                            e-102
gi | 23380177 | gb | AAM83024.1
                                                                       369
                              polymerase [Hepatitis B virus]
                                                                            e-101
gi | 23380072 | gb | AAM82954.1
                              polymerase [Hepatitis B virus]
                                                                       368
                                                                            e-101
gi | 23380084 | gb | AAM82962.1
                                                                       368
                                                                            e-101
                              polymerase [Hepatitis B virus]
gi | 23380078 | gb | AAM82958.1
                                                                       368
gi|23380066|gb|AAM82950.1
                              polymerase [Hepatitis B virus]
                                                                            e-101
                              polymerase [Hepatitis B virus]
                                                                       368
                                                                            e-101
gi | 23380111 | gb | AAM82980.1 |
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polymerase [Hepatitis B virus]
                                                                          367
                                                                                e-101
gi | 23380063 | gb | AAM82948.1 |
                                                                          367
                                                                                e-101
gi | 23380087 | gb | AAM82964.1 |
                               polymerase [Hepatitis B virus]
                                                                          366
                                                                                e-101
                              DNA polymerase [Hepatitis B virus]
gi | 3335627 | gb | AAD13662.1 |
                                                                          366
                                                                                e-101
gi | 23380069 | gb | AAM82952.1 |
                               polymerase [Hepatitis B virus]
                                                                                e-101
                                                                          366
                               polymerase [Hepatitis B virus]
gi|23380090|gb|AAM82966.1
                                                                          366
                                                                                e-101
                               polymerase [Hepatitis B virus]
gi|23380060|gb|AAM82946.1
                               polymerase [Hepatitis B virus]
                                                                          365
                                                                                e-100
gi|23380105|gb|AAM82976.1
gi|23380132|gb|AAM82994.1
                               polymerase [Hepatitis B virus]
                                                                          365
                                                                                e-100
                               polymerase [Hepatitis B virus]
                                                                          365
                                                                                e-100
gi|23380093|gb|AAM82968.1
                               polymerase [Hepatitis B virus]
                                                                          365
gi|23380183|gb|AAM83028.1
                                                                                e - 100
                               polymerase [Hepatitis B virus]
                                                                          365
                                                                                e - 100
gi | 23380120 | gb | AAM82986.1 |
                                                                          365
                                                                                e-100
gi|13991875|gb|AAK51541.1|AF363963_2 truncated polymerase [...
                                                                          363
                                                                                e-100
                               polymerase [Hepatitis B virus]
gi 23380129 gb AAM82992.1
                                                                          363
                                            [Hepatitis B virus]
                                                                                e - 100
gi | 23380186 | gb | AAM83030.1
                               polymerase
                                                                          363
                                                                                e-100
                                            [Hepatitis B virus]
gi|23380168|gb|AAM83018.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          363
                                                                                e - 100
gi|23380075|gb|AAM82956.1
                               polymerase
                               polymerase
                                            [Hepatitis B virus]
                                                                          361
                                                                                3e-99
gi | 23380123 | gb | AAM82988.1
                                                                          357
                                                                                4e-98
gi | 23380135 | gb | AAM82996.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          351
                                            [Hepatitis B virus]
                                                                                3e-96
qi|23380030|qb|AAM82926.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          351
                                                                                3e-96
gi|23380021|gb|AAM82920.1
                               polymerase
                               polymerase
                                            [Hepatitis B virus] >...
                                                                          350
                                                                                8e-96
gi | 23379934 | gb | AAM82862.1
                               polymerase [Hepatitis B virus]
                                                                          349
                                                                                1e-95
gi|23380036|gb|AAM82930.1
                               polymerase [Hepatitis B virus]
gi|23380156|gb|AAM83010.1
                                                                          349
                                                                                1e-95
                               polymerase
                                            [Hepatitis B virus]
                                                                          349
                                                                                1e-95
gi | 23379922 | gb | AAM82854.1
                                            [Hepatitis B virus]
gi|23379943|gb|AAM82868.1
                               polymerase
                                                                          349
                                                                                1e-95
                                                                          349
                                                                                1e-95
gi | 23379967 | gb | AAM82884.1
                               polymerase
                                            [Hepatitis B virus]
                                            [Hepatitis B virus]
                                                                          349
                                                                                1e-95
gi | 23379928 | gb | AAM82858.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          348
                                                                                2e-95
qi | 23380057 | qb | AAM82944.1
                               polymerase
                                                                          348
                                                                                2e-95
                                            [Hepatitis B virus] >...
qi | 23379925 | qb | AAM82856.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          348
                                                                                2e-95
qi | 23380141 | gb | AAM83000.1
                               polymerase
                                                                          348
                                                                                2e-95
qi|23380165|qb|AAM83016.1
                               polymerase
                                            [Hepatitis B virus]
                                            [Hepatitis B virus]
                                                                          348
                                                                                3e-95
qi | 23379997 | qb | AAM82904.1
                               polymerase
qi | 23380147 | gb | AAM83004.1
                               polymerase [Hepatitis B virus]
                                                                          348
                                                                                3e-95
                               polymerase [Hepatitis B virus] >...
                                                                          348
                                                                                3e-95
gi|23379868|gb|AAM82818.1
gi | 23379958 | gb | AAM82878.1 |
                               polymerase
                                            [Hepatitis B virus]
                                                                          348
                                                                                3e-95
gi | 23379904 | gb | AAM82842.1 |
                                            [Hepatitis B virus]
                                                                          347
                                                                                3e-95
                               polymerase
gi | 23379931 | gb | AAM82860.1 |
                                            [Hepatitis B virus]
                                                                          347
                                                                                3e - 95
                               polymerase
gi | 23380159 | gb | AAM83012.1 |
                                            [Hepatitis B virus]
                                                                          347
                                                                                3e - 95
                               polymerase
                                            [Hepatitis B virus]
gi | 23380144 | gb | AAM83002.1 |
                               polymerase
                                                                          347
                                                                                3e-95
                                                                          347
gi | 23379892 | gb | AAM82834.1 |
                               polymerase
                                            [Hepatitis B virus]
                                                                                4e - 95
                                            [Hepatitis B virus]
                                                                          347
                                                                                4e - 95
gi | 23380000 | gb | AAM82906.1 |
                               polymerase
                                                                          347
                                                                                4e-95
gi | 23380042 | gb | AAM82934.1 |
                                            [Hepatitis B virus]
                               polymerase
gi | 23380003 | gb | AAM82908.1 |
                                            [Hepatitis B virus]
                                                                          347
                                                                                5e-95
                               polymerase
                                                                          347
gi | 23379886 | gb | AAM82830.1
                               polymerase
                                            [Hepatitis B virus]
                                                                                5e-95
gi | 23380009 | gb | AAM82912.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          347
                                                                                6e-95
                                                                          347
                                                                                6e-95
gi | 23380153 | gb | AAM83008.1
                               polymerase
                                            [Hepatitis B virus]
gi | 23379973 | gb | AAM82888.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          347
                                                                                6e-95
gi | 23380045 | gb | AAM82936.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          346
                                                                                7e-95
qi | 23379877 | gb | AAM82824.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          346
                                                                                8e-95
qi | 23380138 | qb | AAM82998.1
                                            [Hepatitis B virus]
                                                                          346
                                                                                9e-95
                               polymerase
gi | 23379871 | gb | AAM82820.1
                                            [Hepatitis B virus]
                                                                          346
                                                                                9e-95
                               polymerase
gi | 23380162 | gb | AAM83014.1
                                            [Hepatitis B virus]
                                                                          346
                                                                                9e-95
                               polymerase
gi|23379946|gb|AAM82870.1
                               polymerase
                                            [Hepatitis B virus]
                                                                          346
                                                                                9e-95
gi | 23379895 | gb | AAM82836.1 |
                               polymerase [Hepatitis B virus]
                                                                          346
                                                                                1e-94
gi | 23379913 | gb | AAM82848.1 |
                               polymerase [Hepatitis B virus]
                                                                          345
                                                                                1e-94
                               polymerase [Hepatitis B virus]
gi | 23379916 | gb | AAM82850.1 |
                                                                          345
                                                                                1e-94
gi|23379991|gb|AAM82900.1|
                               polymerase [Hepatitis B virus]
                                                                          345
                                                                                1e-94
gi|23380012|gb|AAM82914.1
                               polymerase [Hepatitis B virus]
                                                                          345
                                                                                1e-94
gi|23379889|gb|AAM82832.1
                               polymerase [Hepatitis B virus]
                                                                          345
                                                                                1e-94
gi | 23379949 | gb | AAM82872.1 |
                               polymerase [Hepatitis B virus]
                                                                          345
                                                                                1e-94
```

```
qi | 23380039 | gb | AAM82932.1 |
                               polymerase [Hepatitis B virus]
qi | 23379898 | qb | AAM82838.1 |
                               polymerase [Hepatitis B virus]
                                                                         345
                                                                               2e-94
gi | 23379880 | gb | AAM82826.1 |
                               polymerase [Hepatitis B virus]
                                                                         345
                                                                               2e-94
                               polymerase [Hepatitis B virus]
gi | 23380033 | gb | AAM82928.1 |
                                                                         345
gi | 23379874 | gb | AAM82822.1 |
                               polymerase [Hepatitis B virus]
                                                                         344
                                                                               3e-94
                               polymerase [Hepatitis B virus]
                                                                         344
                                                                               3e-94
gi | 23379979 | gb | AAM82892.1 |
gi | 23380015 | gb | AAM82916.1 |
                               polymerase [Hepatitis B virus]
                                                                         344
                                                                               4e-94
gi|23379937|gb|AAM82864.1|
                               polymerase [Hepatitis B virus]
                                                                         344
                                                                               4e-94
                                                                         343
gi | 23379940 | gb | AAM82866.1 |
                               polymerase [Hepatitis B virus] >...
                                                                               5e-94
gi | 23380054 | gb | AAM82942.1 |
                               polymerase [Hepatitis B virus]
                                                                         343
                                                                               7e-94
qi | 23379910 | gb | AAM82846.1 |
                               polymerase [Hepatitis B virus]
                                                                         343
                                                                               7e-94
gi | 23379901 | gb | AAM82840.1 |
                               polymerase [Hepatitis B virus]
                                                                         343
                                                                               8e-94
gi | 23380018 | gb | AAM82918.1 |
                               polymerase [Hepatitis B virus]
                                                                         343
                                                                               9e-94
                               polymerase [Hepatitis B virus]
                                                                         342
                                                                               1e-93
qi | 23380027 | gb | AAM82924.1 |
gi | 1914714 | emb | CAA66689.1 |
                               polymerase [Hepatitis B virus]
                                                                         342
                                                                               1e-93
gi | 23379982 | gb | AAM82894.1 |
                              polymerase [Hepatitis B virus]
                                                                         342
                                                                               2e-93
gi | 5019986 | gb | AAD37962.1 |
                              P protein [Hepatitis B virus]
                                                                         341
                                                                               2e-93
gi | 23380051 | gb | AAM82940.1 |
                              polymerase [Hepatitis B virus]
                                                                         341
                                                                               2e-93
gi|27450186|gb|AA014550.1|AF460223_1 polymerase [Hepatitis ...
                                                                         341
                                                                               3e-93
gi | 5019949 | gb | AAD37932.1 |
                             P protein [Hepatitis B virus]
                                                                         341
                                                                               4e-93
gi|27450210|gb|AA014562.1|AF460235_1 polymerase [Hepatitis ...
                                                                         338
                                                                               2e-92
                                        polymerase [Hepatitis ...
gi | 27450206 | gb | AAO14560.1 | AF460233_1
                                                                         337
                                                                               4e-92
                              polymerase [Hepatitis B virus]
                                                                         336
                                                                               7e-92
gi | 1107593 | emb | CAA56885.1 |
gi|27450208|gb|AAO14561.1|AF460234_1 polymerase [Hepatitis ...
                                                                         336
                                                                               8e-92
gi|27450182|gb|AA014548.1|AF460221 1
                                         polymerase [Hepatitis ...
                                                                         336
                                                                               8e-92
gi|27450184|gb|AA014549.1|AF460222_1 polymerase [Hepatitis ...
                                                                         335
                                                                               2e-91
gi | 3820918 | emb | CAA08937.1 |
                              polymerase [Hepatitis B virus] >...
                                                                         332
                                                                               2e-90
                              polymerase [Hepatitis B virus]
qi | 3820942 | emb | CAA08951.1 |
                                                                         330
                                                                               5e-90
gi | 3820933 | emb | CAA08947.1 |
                              polymerase [Hepatitis B virus]
                                                                         326
                                                                               8e-89
gi | 3820945 | emb | CAA08953.1 |
                              polymerase [Hepatitis B virus]
                                                                         326
                                                                               9e-89 ·
gi | 3820930 | emb | CAA08945.1 |
                              polymerase [Hepatitis B virus]
                                                                         325
                                                                               3e-88
```

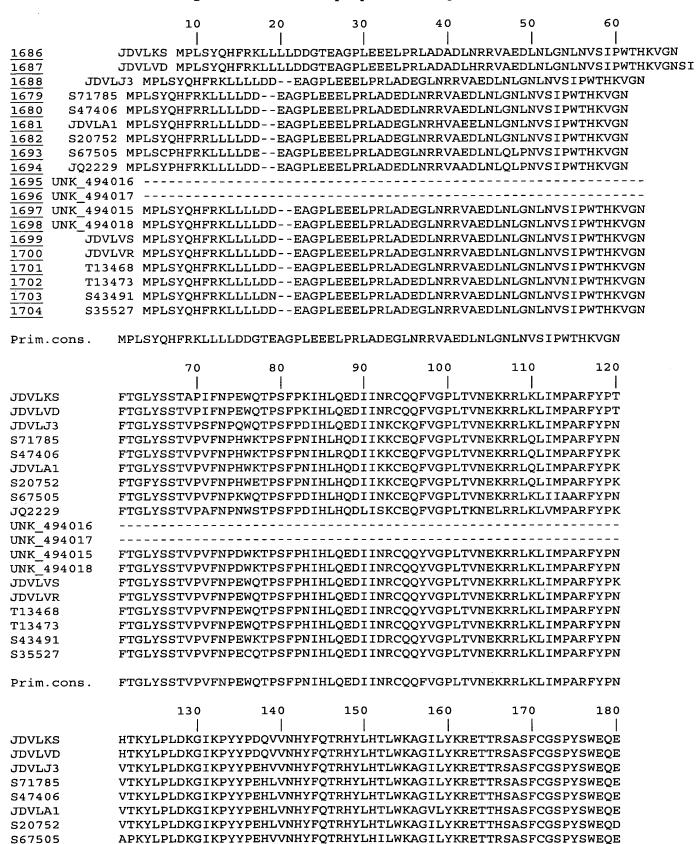
345

1e-94

```
Query= gi | 93080 | pir | | S20757 DNA-directed DNA polymerase (EC
2.7.7.7) - hepatitis B virus (subtype ayw, patient E)
         (832 letters)
cutoff = 3e-88
Database: All non-redundant GenBank CDS
translations+PDB+SwissProt+PIR+PRF
           1,376,942 sequences; 442,405,847 total letters
```

BLASTP 2.2.5 (Nov-16-2002) (Altschul, S.F., et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402 (1997)) against HBV subtype sequence S20757, cutoff = 3e-88 (to select human sequences).

Table 21: CLUSTALW alignment of 19 HBV polymerase sequences

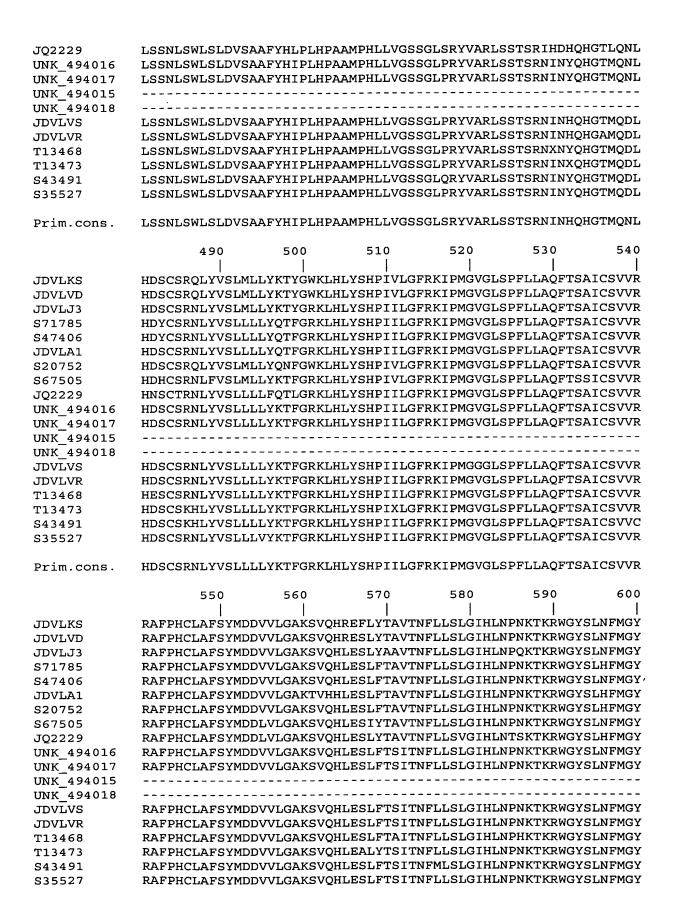


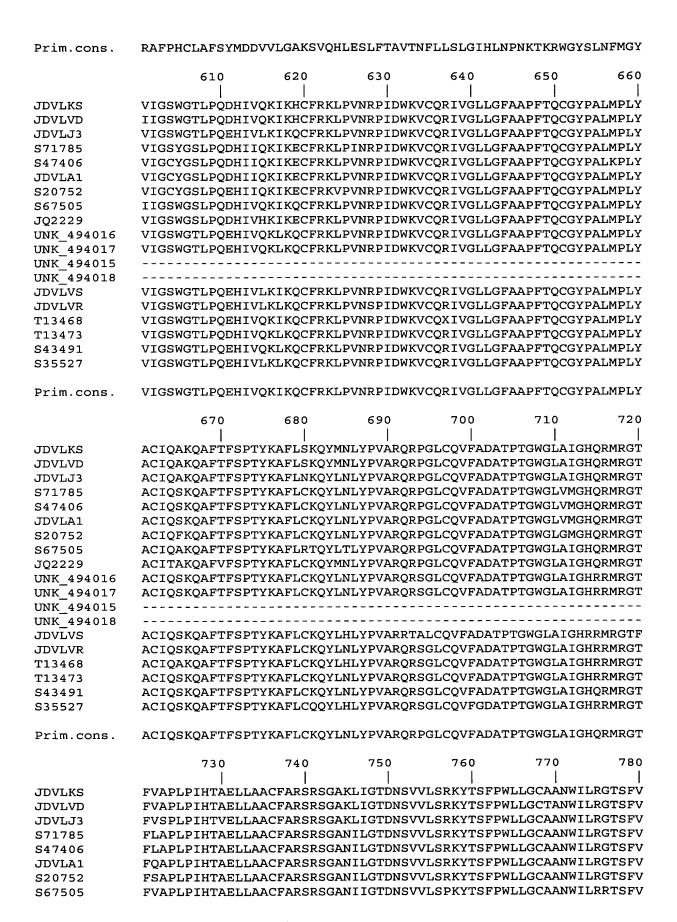
JQ2229 UNK 494016	VTKYFPMDKGIKPY	YPEHAVNHYF	KTRHYLHTLWK	(AGILYKREST	RSASFCGSPYSWEQE
_			_		
UNK_494017	T THE TAX DE DESCRIPTION			A GIL VEDERM	DCA GECCCDVCWEOE
UNK_494015					RSASFCGSPYSWEQE
UNK_494018					RSASFCGSPYSWEQE
JDVLVS					RSASFCGSPYSWEQE
JDVLVR					RSASFCGSPYSWEQE
T13468					RSASFCGSPYSWEQE
T13473					'RSASFCGSPYSWEQE
S43491					RSASFCGSPYSWEQE
S35527	LTKYLPLDKGIKPY	YPEHAVNHYF	KTRHYLHTLWK	KAGILYKRETT	RSASFCGSPYSWEQE
Prim.cons.	LTKYLPLDKGIKPY	YPEHAVNHYF	QTRHYLHTLWK	KAGILYKRETT	RSASFCGSPYSWEQE
	190 	200 	210 	220 	230 240
JDVLKS	I.OHGRI.VIKTSORH	GDESECSOPS	GTLSRSSVGPC	TRSOLKOSRL	GLQPHQGPLASSQPG
JDVLVD					GLQPRQGRLASSQPS
JDVLJ3					GPQPTQGQLAGLQQG
S71785					GLQSQQGHLARRQQG
S47406					GLQSQQGHLARRQQG
JDVLA1					GLQSQQGLLARRQQG
S20752					GLQSQQGHLARRQQG
S67505					GLQSQQRQLARSHQG
JQ2229					GLQHKQGQLANGKQG
UNK 494016	LQNG313LND1KKI	GIESHCAQSS			
UNK 494017					
UNK 494015	T.OUGDT.VEOTGTDE	COFCECCOSS	CTT.SPSDVCDC	WPSOLKOSPI.	GLQPQQGSLARGKSG
UNK 494018					GLQPQQGSLARGKSG
JDVLVS					GLQPQQGSLARGKSG
JDVLVS					GLQPQQGSMARGKSG
T13468					GLQPQQGSLARGKSG
T13473					GLQPQQGSLARGQSG
S43491					GLQPQQGSLARGKAG
S35527					GLQPQQGSLARRNQG
055527	EQUOREVIQUO	.02251 05405			
Prim.cons.	LQHGRLVFQTSTRH	IGDESFCSQSS	GILSRSPVGPC	CVRSQLKQSRL	GLQPQQGSLARGQQG
	250	260	270	280	290 300
JDVLKS	RSGSIRARVHPSTF	RCFGVEPSGS	GHVDPSVNNSS	SSCLRQSAVRK	AAYSHLSTSKRQSSS
JDVLVD					AAYSHLSTSKRQSSS
JDVLJ3					EAYSPVSTSKRHSSS
S71785	RSWSIRAGIHPTAF	RPFGVEPSGS	GHNTNLASKS#	ASCIYQSPVRK	AAYPAVSTFEKHSSS
S47406	RSWSIRAGIHPTAF	RPFGVEPSGS	GHNTNLASKS#	ASCLYQSPVRK	AAYPAVSTFEKHSSS
JDVLA1	RSWSIRAGIHPTAF	RPFGVEPSGS	GHTTNLASKS#	ASCLHQSPVRK	ATYPSVSTFEKHSSS
S20752	WSWSIRAGTHPTAF	RPFGVEPSGS	GHTTHRASKS#	ASCLYQSPDRK	ATYPSVSTFERHSSS
S67505	RSGSIRARVHSTT	RSFRVELSGS	GSNHNIASTSS	SCRHQSAVRE	TAYSHLSTVERHSSS
JQ2229	RSGRLRSRVHTPTF	WPAGVEPSST	RCVNNLASRSA	ASCFHQSAVRE	KANPSLSTSKRHTST
UNK 494016		. 		- 	
UNK 494017					
UNK_494015	RSGSIWSRVHPTTF	RPFGVEPSGS	GHIDNTASSTS	SCLHQSAVRK	TAYSHLSTSKRQSSS
UNK_494018	RSGSIWSRVHPTTF	RPFGVEPSGS	GHIDNTASSTS	SSCLHQSAVRK	TAYSHLSTSKRQSSS
JDVLVS	RSGSIRARVPPTTF	RRSFGVEPSGS	GHIDNRASSTS	SCLHQSAVRK	TAYSHLSTSKRQSSS
JDVLVR	RSGSIRARVHPTTF	RSFGVEPSGS	GHIDNSASSTS	SSCLHQSAVRK	TAYSHLSTSKRQSSS
T13468	RSGSIRARVHPTT	RSFGVEPSGS	GHIDNSARSAS	SSCLHQSAVRK	TAYSHLSTSKRQSSS
T13473					TAYCHLSTTKRQSSS
S43491	RSGSIRARVHPTTF	RRPFGVEPSGS	GHIDNSASSAS	SSCFHQSAVRK	TAYSHLSTSKRQSSS
S35527	RSGRLRARVHPTTF	RRSFGVEPSGS	GHLDNSASSSS	SSCLHQSAVRK	TAYSHLSTSKRQSSS

RSGSIRARVHPTTRRPFGVEPSGSGHIDNSASSSSSCLHQSAVRKTAYSHLSTSKRQSSS Prim.cons. 350 360 340 310 320 330 GHAVEFHCLPPSSARPQSQGSVFSCWWLQFRNSKPCSEYCLSHLVNLREDRGPCDEHGEH **JDVLKS** GHAVEFHCLPPNSAGSQSQGSVSSCWWLQFRNSKPCSEYCLSHLVNLREDWGPCDEHGEH **JDVLVD** GNAVELHHVPPNSSRSQSQGSVLSCWWLQFRNSKPCSEHCLFHIVNLIDDWGPCAEHGEH JDVLJ3 GHAVELHNFPPNSARSQGERPVFPCWWLQFRNSKPCSDYCLSHIVNLLEDWGPCTEHGEH S71785 GHAVELHNLPPNSSRSQGERPVFPCWWLQFRNSKPCSDYCLSHIVNLLEDWGPCAEHGEH S47406 GHAVELHNLPPNSARSQSERPVSPCWWLQFRNSKPCSDYCLSHIVNLLEDWGPCAEHGEH JDVLA1 GRAVELHNFPPNSARSQSERPIFPCWWLQFRNSKPCSDYCLSLIVNLLEDWGPCDEYGEH S20752 GHEVELYSIPPNSARSQSTGPILSCWWLQFRNSEPCSDYCLSHLVNLLEDWGPCTEHGEH S67505 GNAVELNPVPPSSVGSQGKGSVLPCWWLQFRDTEPCSDYCLSHIINLLEDWGPCYEHGQH JQ2229 ----LHNIPPSSARSQSEGPIFSCWWLQFRNSKPCSDYCLTHIVNLLEDWGPCTEHGEH UNK 494016 ----LHNIPPSSARSQSEGPIFSCWWLQFRNSKPCSDYCLTHIVNLLEDWGPCTEHGEH UNK_494017 UNK_494015 UNK_494018 GHAVE--------**JDVLVS** GHAVELHHISPSPARSQSEGPIFSSWWLQFRNSKPCSDYCLTHIVNLLEDWGPCTEHGEH GHAVEFHNIPPSSARSQSEGPIFSCWWLQFRNSKPCSDYCLTHIVNLLEDWGPCTEHGEH **JDVLVR** GHAVELHPCWWLOFRNSKPCSDYCLTHIVNLLEDWGPCTEHGEHNIRIPRTPARVTGGVF T13468 GHAVETCWWLOFRNSKPCSDYCLTHIVNLLEDWGPCTEHGEHNIRIPRTPARVTGGVFLV T13473 GHAVELHNIPPSSARSKSEGPLFPCWWLQFRNSKPCSDYCLTHIVNLLEDWGPCTEHGEH S43491 GHAVELHNIPPSSARSQSEGPIFSCWWLQFRNSKPCSDYCLTHIVNLLEDWGPCTEHGEH S35527 GHAVELHNIPPSSARSQSEGP2FSCWWLQFRNSKPCSDYCLSHIVNLLEDWGPCTEHGEH Prim.cons. 400 410 420 390 370 380 HIRIPRTPARVTGGVFLVDKNPHNTAESRLVVDFSQFSRGITRVSWPKFAIPNLQSLTNL **JDVLKS** HIRIPRTPARVTGGVFLVDKNPHNTAESRLVVDFSQFSRGISRVSWPKFAVPNLQSLTNL **JDVLVD** RIRTPRTPARVTGGVFLVDKNPHNTSESRLVVDFSQFSRGNTRVSWPKFAVPNLQSLTNL JDVLJ3 HIRIPRTPARVTGGVFLVDKNPHNTAESRLVVDFSQFSRGNHRVSWPKFAVPNLQSLTNL S71785 HIRIPATPARVTGGVFLVDKNPHNTAESRLVVDFSQFSRGNYRVSWPKFAVPNLQSLTNL S47406 HIRIPATPARVTGGVFLVDKNPHNTEESRLVVDFSQFSRGNHRVSWPKFAVPNLQSLTNL JDVLA1 HIRIPRTPARVTGGVFLVDKNPHNTAESRLVVDFSQFSRGNYRVSWPKFAVPNLQSLTNL S20752 HIRIPATPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGSTRVSWPKFAVPNLQSLTNL S67505 YIRTPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGTTRVSWPKFAVPNLQSLTNL JQ2229 NIRIPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGSTHVSWPKFAVPNLQSLTNL UNK 494016 NIRIPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGSTHVSWPKFAVPNLQSLTNL UNK_494017 UNK 494015 UNK_494018 $\verb"NIRIPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGSTHVSWPKFAVPNLQSLTNL"$ **JDVLVS** NIRIPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGSTHVSWPKFAVPNLQSLTNL **JDVLVR** LVDKNPHNTTESRLVVDFSQFSRGSTX--------VSWPKFAVPNLQSLTNL T13468 DKNPHNTTESX----------LVVDFSQFSRGSTQVSWPKFAVPNLQSLTNL T13473 NIRIPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGNTQVSWPKFAVPNLQSLTNL S43491 NIRIPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGSTHVSWPKFAVPNLQSLTNL S35527 HIRIPATPARVTGGVFLVDKNPHNTTESRLVVDFSQFSRGSTRVSWPKFAVPNLQSLTNL Prim.cons. 450 460 470 480 430 440 LSSNLSWLSLDVSAAFYHIPLHPAAMPHLLIGSSGLSRYVARLSSNSRINNNQYGTMQNL **JDVLKS** LSSNLSWLSLDVSAAFYHIPLHPAAMPHLLIGSSGLSRYVARLSSNSRINNNQYGTMQNL JDVLVD LSSDLSWLSLDVSAAFYHLPLHPAAMPHLLVGSSGLSRYVARLSSNSRIINHQHRTMQNL JDVLJ3 LSSNLSWLSLDVSAAFYHLPLHPASMPHLLVGSTGLSRYVARVSSNSRIFNHQRGTMQNL S71785 LSSNLSWLSLDVSAAFYHLPLHPAAMPHLLVGSSGLSRYVARLSSNSRIFNNQRGTMQNL S47406 LSSNLSWLSLDVSAAFYHLPLHPAAMPHLLVGSSGLSRYVARLSSDSRIFNHQHGTMQNL JDVLA1 LSSNLSWLSLDVSAGFYHLPLHPAAMPHLLVGSSGVSRYVARLSSNSRNNNNQYGTMQNL S20752

S67505

LSSNLSWLSLDVSAAFYHLPLHPAAMPHLLVGSSGLSRYVARLSSTSRIIDHQHGTMQNL





JQ2229	FVAPLPIHTAELLAACFARSRSGATLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
UNK 494016	FVAPLPIHTAELLAACFARSRSGAKLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
UNK 494017	FVAPLPIHTAELLAACFARSRSGAKLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
UNK 494015	
UNK 494018	
JDVLVS	VAPLPIHTAELLAACFARSRSGAKLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTYFVY
- - · - · -	FVAPLPIHTAELLAACFARSRSGAKLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
JDVLVR	
T13468	FVAPLPIHTAELLAACFARSRSGAKLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
T13473	FVAPLPIHTAELLAACFARSRSGAKLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
S43491	FVAPLPIHTAELLAACFARSRSGATLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
S35527	FVAPLPIHTAELLAACFARSRSGAKLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
Prim.cons.	FVAPLPIHTAELLAACFARSRSGAKLIGTDNSVVLSRKYTSFPWLLGCAANWILRGTSFV
	790 800 810 820 830 840
JDVLKS	YVPSALNPADDPSRGRLGLSRPLLRLPFQPTTGRTSLYAVSPSVPSHLPVRVHFASPLHV
	YVPSALNPADDPSRGRLGLSRPLLRLPFQPTTGRTSLYAVSPSVPSHLPVRVHFASPLHV
JDVLVD	~
JDVLJ3	YVPSALNPADDPSRGRLGLYRPLLRLPYRPTTGRTSLYADSPSVPSHLPDRVHFASPLHV
S71785	YVPSALNPADDPSRGRLGIFRPLLRLPFRPTTGRTSLYADSPSVPSHLPVRVHFASPLHV
S47406	YVPSALNPADDPSRGRLGLSRPLLRLPFRPTTGRTSLYADSPSVPSHLPDRVHFASPLHV
JDVLA1	YVPSALNPADDPSRGRLGLSRPLLRLPFRPTTGRTSLYADSPSVPSHLPDRVHFASPLHV
S20752	YVPSALNPADDPSRGRLGLSRPLLCLPFRPTTGRTSLYADSPSVPSHLPDRVHFASPLHV
S67505	YVPSALNPADDPSRGRLGLYRPLLRPWFRPTTGRTSLYAVSPSVPSHLPVRVHFASPLHV
JQ2229	YVPSALNPADDPSRGRLGLYRPLLRLPFQPTTGRTSLYADSPSVPSHLPDRVHFASPLHV
UNK_494016	YVPSALNPADDPSRGRLGLYRPLLHLPFRPTTGRTSLYAVSPSVPSHLPDRVHFASPLHV
UNK 494017	YVPSALNPADDPSRGRLGLYRPLLHLPFRPTTGRTSLYAVSPSVPSHLPDRVHFASPLHV
UNK 494015	
UNK 494018	
JDVLVS	VPSALNPADDPSRGRLGLIRPLLHLRFRPTTGRTSLYAVSPSVPSHLPDRVHFASPLHVA
JDVLVR	YVPSALNPADDPSRGRLGLYRPLLLLPFRPTTGRTSLYAVSPSVPSHLPDRVHFASPLHV
T13468	YVPSALNPADDPSRGRLGLYRPLLHLPFRPTTGRTSLYAVSPSVPSHLPDRVHFASPLHV
T13473	YVPSALNPADDPSRGRLGLYRPLLHLPFRPTTGRTSLYAVSPSVPSHLPDRVHFASPLHV
S43491	YVPSALNPADDPSRGRLGLYRPLLRLSFRPTTGRTSLYAVSPSVPSHLPDRVHFASPLHV
S35527	YVPSALNPADDPSRGRLGLYRPLLHLPFQPTTGRTSLYAVSPSVPSHLPVRVHFASPLHV
535527	1VPSAUMPADDPSRGRUGUIRFUUMUFFQFIIGRIOUIAVOF5VFOMUFVRVINFASFUMV
Prim.cons.	YVPSALNPADDPSRGRLGLYRPLLRLPFRPTTGRTSLYAVSPSVPSHLPDRVHFASPLHV
JDVLKS	AWRPP
JDVLVD	AWRPP
JDVLJ3	AWRPP
S71785	AWRPP
S47406	AWRPP
JDVLA1	AWRPP
S20752	AWRPP
S67505	AWRPP
JQ2229	AWRPP
UNK 494016	AWRPP
UNK 494017	AWRPP
UNK 494017	
UNK_494018	WDDD_
JDVLVS	WRPP-
JDVLVR	AWRPP
T13468	AWRPP
T13473	AWRPP
S43491	AWRPP
S35527	AWRPP

Prim.cons. AWRPP

CLUSTALW alignment of 19 HBV polymerare sequences representing the sybtypes adw (4), ayw (5), ayr (4) and adr (6) (NPS@: Network Protein Sequence Analysis, TIBS Vol. 25, No 3 (291):147-150, Combet C., Blanchet C., Geourjon C. and Deléage G. (March 2000))

CLUSTALW options used :
endgaps=1
gapdist=8
gapext=0.2
gapopen=10.0
hgapresidues=GPSNDQERK
ktuple=1
matrix=gonnet
maxdiv=30
outorder=aligned
pairgap=3
score=percent
topdiags=5
type=PROTEIN
window=5

Table 22. HCV Multiple Sequence Alignment GCG Multiple Sequence File. Written by Omiga 1.1

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	ED43type_4			3052	Check:		Weight:	
		SEQ ID NO: 1710		3052	Check:		Weight:	
	HC_C2	SEQ ID NO: 1710		3052	Check:		Weight:	
	HC_G9	SEQ ID NO: 1709 SEQ ID NO: 1711		3052	Check:		Weight:	
	HCU16326				Check:		Weight:	
	HCV_H_CMR	SEQ ID NO: 1712		3052				
	HCV_J1	SEQ ID NO: 1713		3052	Check:		Weight:	
	HCV_J483	SEQ ID NO: 1714		3052	Check:		Weight:	
	HCV_J8	SEQ ID NO: 1715		3052	Check:		Weight:	
	HCV_JK1	SEQ ID NO: 1716		3052	Check:		Weight:	
	HCV_JS	SEQ ID NO: 1717		3052	Check:		Weight:	
	HCV_K1_R1	SEQ ID NO: 1718		3052	Check:		Weight:	
	HCV_K1_R2	SEQ ID NO: 1719		3052	Check:		Weight:	
	HCV_K1_R3	SEQ ID NO: 1720		3052	Check:		Weight:	
	HCV_K1_S1	SEQ ID NO: 1721		3052	Check:		Weight:	
Name:	HCV_K1_S2	SEQ ID NO: 1722		3052	Check:		Weight:	
	HCV_K1_S3	SEQ ID NO: 1723		3052	Check:		Weight:	
Name:	HCV_L2	SEQ ID NO: 1724	Len:	3052	Check:		Weight:	1.00
Name:	HCV_N	SEQ ID NO: 1725	Len:	3052	Check:	1702	Weight:	
Name:	HCV12083	SEQ ID NO: 1726	Len:	3052	Check:		Weight:	
Name:	HCV1480	SEQ ID NO: 1727	Len:	3052	Check:	5620	Weight:	1.00
Name:	HCVPOLYP	SEQ ID NO: 1728	Len:	3052	Check:	2663	Weight:	1.00
Name:	HD_1	SEQ ID NO: 1729	Len:	3052	Check:	4040	Weight:	1.00
Name:	HPCCGAA	SEQ ID NO: 1730	Len:	3052	Check:	5414	Weight:	1.00
Name:	HPCFG	SEQ ID NO: 1731	Len:	3052	Check:	7119	Weight:	1.00
Name:	HPCGENANTI	SEQ ID NO: 1732	Len:	3052	Check:	9591	Weight:	1.00
Name:	HPCGENOM	SEQ ID NO: 1733	Len:	3052	Check:	2009	Weight:	1.00
Name:	HPCHUMR	SEQ ID NO: 1734	Len:	3052	Check:	4863	Weight:	1.00
Name: H		SEQ ID NO: 1735	Len:	3052	Check:	3553	Weight:	1.00
Name:	HPCJCG	SEQ ID NO: 1736	Len:	3052	Check:	6658	Weight:	1.00
	HPCJK046	SEQ ID NO: 1737	Len:	3052	Check:	436	Weight:	
	HPCJK049	SEQ ID NO: 1738	Len:	3052	Check:		Weight:	
	HPCJTA	SEQ ID NO: 1739		3052	Check:	2902	Weight:	
	HPCJTB	SEQ ID NO: 1740		3052	Check:		Weight:	
	HPCK3A	SEQ ID NO: 1741		3052	Check:	2180	Weight:	
	HPCPLYPRE	SEQ ID NO: 1742		3052	Check:		Weight:	
	HPCPOLP	SEQ ID NO: 1743		3052	Check:	1218	Weight:	
	HPCPP	SEQ ID NO: 1744		3052	Check:		Weight:	
	HPCUNKCD	SEQ ID NO: 1745		3052	Check:		Weight:	
	MKC1A	SEQ ID NO: 1746		3052	Check:		Weight:	
	NDM59	SEQ ID NO: 1747			Check:		_	
Name:		SEQ ID NO: 1748		3052	Check:		Weight:	
Name:		SEQ ID NO: 1749		3052	Check:		Weight:	
Name:	Th580	SEQ ID NO: 1750		3052	Check:		Weight:	
		SEQ ID NO: 1751		3052	Check:		Weight:	
		SEQ ID NO: 1751		3052	Check:		Weight:	
	TypeV_D VN004	SEQ ID NO: 1752 SEQ ID NO: 1753		3052	Check:		Weight:	
		SEQ ID NO: 1754		3052	Check:		Weight:	
	VN235	SEQ ID NO: 1754 SEQ ID NO: 1755		3052	Check:		Weight:	
name:	VN405	2EG ID NO: 1/22	пен:	3032	CHECK:	1443	werdur:	1.00

1709	HC_C2	MSTNPKPQRK	TKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1710</u>	HC_G9				VGGVYLLPRR	
<u>1711</u>	HCU16326	MSTNPKPQRK	TKRNTNRRPQ	DIKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1712</u>	HCV_H_CMR	·-			VGGVYLLPRR	
<u>1713</u>	HCV_J1	MSTIPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1714	HCV_J483	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1715</u>	HCV_J8	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1716</u>	HCV_JK1	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1717</u>	HCV_JS	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1718</u>	HCV_K1_R1	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1719</u>	HCV_K1_R2	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1720</u>	HCV_K1_R3	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1721</u>	HCV_K1_S1	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1722	HCV_K1_S2	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1723</u>	HCV_K1_S3	MSTNPKPQRQ	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1724	HCV_L2	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1725</u>	HCV_N	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	EVKFPGGGQI	VGGVYLLPRR	GPRLGVRAIR
<u>1726</u>	HCV12083	MSTLPKPQRK	${\tt TKRNTNRRPM}$	DVKFPGGGQI	VGGVYLLPRK	GPRLGVRATR
1727	HCV1480	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPKLGVRATR
1728	HCVPOLYP	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRALR
<u>1729</u>	HD_1	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1730</u>	HPCCGAA	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1731	HPCFG	MSTLPKPKRQ	${\tt TKRNTLRRPK}$	NVKFPAGGQI	VGEVYVLPRR	GPQLGVREVR
1732	HPCGENANTI	MSTNGKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1733</u>	HPCGENOM	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1734</u>	HPCHUMR	MSTNPKPQRK	TKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRAPR
1735	HPCJ	MSTNPKPQRK	${\tt TKRNTNRRPQ}$	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1736	HPCJCG	MSTNPKPQRK	TKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1737	HPCJK046	MSTNPKPQRQ	TKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1738</u>	HPCJK049	MSTLPKPQRI	TKRNINRRPQ	DVKFPGGGQI	VGGVYVLPRR	GPKLGVRAVR
1739	HPCJTA	MSTNPKPQRK	TKRNTYRRPQ	DVKFPGGGQI	VGGVYVLPRR	GPTLGVRATR
1740	HPCJTB	MSTNPKPQRK	TKRNTYRRPQ	DVKFPGGGQI	VGGVYVLPRR	GPTLGVRATR
<u>1741</u>	HPCK3A	MSTLPKPQRK	TKRNTIRRPQ	DVKFPGGGVI	YVGVYVLPRR	GPRLGVRATR
1742	HPCPLYPRE	MSTNPKPQKK	NKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1743	HPCPOLP	MSTNPKPQRK	TKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1744	HPCPP	MSTNPKPQRK	IKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1745</u>	HPCUNKCD	MSTNPKPQRK	TKRNTNRRPQ	DIKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1746	MKC1A	MSTNPKPQRK	IKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1747	NDM59	MSTNPKPQRK	TKRNTSRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
1748	NZLI	MSTLPKPQRK	TKRNTIRRPQ	DVKFPGGGQI	VGGVYVLPRR	GPRLGVRATR
1749	SA13	MSTNPKPQRK	TKRNTNRRPQ	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR
<u>1750</u>	Th580				VGGVYLLPRR	
1751	Type_3a_CB				VGGVYVLPRR	
<u>1752</u>	TypeV_D	MSTLPKPQRK	TKRNTIRRPQ	DVKFPGGGQI	VGGVYVLPRR	GPRLGVRATR
<u>1753</u>	VN004	-			VGGVYLLPRR	
1754	VN235				VGGVYLLPRR	
<u> 1755</u>	VN405	MSTLPKPQRK	TKRNTNRRPM	DVKFPGGGQI	VGGVYLLPRR	GPRLGVRATR

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D89815		RRQPIPKARR			LGWAGWLLSP
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HC C2		RRQPIPKARR		YPWPLYGNEG	MGWAGWLLSP
HC G9		RRQPIPKARR		YPWPLYGNEG	CGWAGWLLSP
HCU16326	KTSERSQPRG	RRQPIPKARR	PEGRAWAQPG	YPWPLYGNEG	LGWAGWLLSP
HCV H CMR		RRQPIPKARR		YPWPLYGNEG	CGWAGWLLSP
HCV J1	KTSERSQPRG	RRQPIPKVRR	PEGRTWAQPG	YPWPLYGNEG	CGWAGWLLSP
HCV_J483	KTSERSQPRG	WRQPIPKARR	PEGRAWAQPG	YPWPLYGNEG	LGWAGWLLSP
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HCV JK1	KTSERSQPRG	RRQPIPKARQ	PEGRAWAQPG	YPWPLYGNEG	LGWAGWLLSP
$HC\overline{V}$ JS	KTSERSQPRG	RRQPIPKARR	PEGRTWAQPG	YPWPLYGNEG	MGWAGWLLSP
HCV_K1_R1	KTSERSQPRG	RRQPIPKARR	PEGRAWAQPG	YPWPLYGNEG	LGWAGWLLSP
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HCV K1 R3	KTSERSQPRG	RRQPIPKVRR	SEGRTWAQPG	YPWPLYGNEG	LGWAGWLLSP
HCV K1_S1	KTSERSQPRG	RRQPIPKARR	PEGRAWAQPG	YPWPLYGNEG	LGWAGWLLSP
HCV_K1_S2	KTSERSQPRG	RRQPIPKARQ	PEGRAWAQPG	YPWPLYGNEG	MGWAGWLLSP
HCV K1 S3	KTSERSQPRG	RRQPIPKVRR	SEGRTWAQPG	YPWPLYGNEG	LGWAGWLLSP
HCV L2	KTSERSQPRG	RRQPIPKARQ	PEGRAWAQPG	YPWPLYANEG	LGWAGWLLSP
HCV N	KTSERSQPRG	RRQPIPKARR	PEGRAWAQPG	YPWPLYGNEG	MGWAGWLLSP
HCV12083	KTSERSQPRG	RRQPIPKARQ	PQGRHWAQPG	YPWPLYGSEG	CGWAGWLLSP
HCV1480	KNSERSQPRG	RRQPIPKARR	PTGRSWGQPG	YPWPLYANEG	LGWAGWLLSP
HCVPOLYP	KTSERSQPRG	RRQPIPKARR	PEGRAWAQPG	YPWPLYGNEG	MGWAGWLLSP
HD 1	KTSERSQPRG	RRQLIPKARQ	PEGRSWAQPG	YPWPLYGNEG	MGWAGWLLSP
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HPCFG	KTSERSQPRG	RRQPTPKARP	REGRSWAQPG	YPWPLYGNEG	CGWAGWLLPP
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NDM59	KTSERSQPRG	RRQPIPKDRR	STGKSWGKPG	YPWPLYGNEG	LGWAGWLLSP
NZLI		RRQPIPKARR			
SA13		RRQPIPKARQ			
Th580		RRQPIPKARP			
Type_3a_CB		RRQPIPKARQ			
TypeV_D		RRQPIPKARR			
VN004		RRQPIPKARQ			
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VN405	KTSERSQPRG	RRQPIPKARQ	SQGRHWAQPG	YPWPLYGNEG	CGWAGWLLSP
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D89815		DPRRRSRNLG			
ED43type_4		DPRGRSRNLG			
HC_C2	RGSRPSWGPN	DPRRRSRNLG	KVIDTLTCGF	ADLMGYIPLV	GAPLGGAARA
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Th580				TTLVLSSILR	
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VN235	VVQDCNCSIY	VGHITGHRMA	WDMMMNWSPT	ATLVLSYVMR	IPQVIMDIFT
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HCU16326

HCV H CMR

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SA13					
Th580		TNVDQDLVGW			
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TypeV_D		TNVDQDLVGW			
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VN235		TNVDQDMVGW			
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HC_C2		LLSPRPISYL			
HC_G9		LLPPRPVSYL			
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  HPCPOLP RDEVSFCVGL NSFVVGSQLP CDPEPDTDVL TSMLTDPSHI TAETAARRLA
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    NDM59 RDEVSFCVGL NSFVVGSQLP CDPEPDADVL TSMLTDPSHI TAEAAARRLA
     NZLI RDDITFMVGL HSYTIGSQLP CEPEPDVSVL TSMLRDPSHI TAETAARRLA
     SA13 REEVCFSVGL HSFVVGSQLP CEPEPDVTVL TSMLSDPAHI TAETAKRRLD
    Th580 RDEVSFSVGL LEFVVGSQLP CEPEPDVTVV TSMLTDPSHI TAETASRRLK
Type_3a_CB REEITFSVGL NSYTIGSQLP CEPEPDVSVL TSMLRDPSHI TAETAARRLA
  TypeV_D RDDITFMVGL NSYAIGSQLP CEPEPDVSVL TSMLRDPSHI TAETAARRLA
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VN004 RDEVSFSVGL SSYAVGSQLP CEPEPDVTVV TSMLIDPSHV TAEAAARRLA
     VN235 RDDITFSVGL STYVVGSQLP CEPEPDVVIL TSMLTDPDHI TAETAARRLA
     VN405 RDEISFLVGL NSYAIGSOLP CEPEPDVTVV TSMLVDPSHL TAEAAARRLA
                                                               2250
    BEBE1 RGSPPSAASS SASOLSAPSL RATCTTHAK. ...CPDIDMV DANLFCWCTM
    D89815 RGSPPSLAGS SASOLSALSL KATCTTHHG. ...APDTDLI EANLLWRQEM
ED43type 4 RGSRPSLASS SASQLSPRLL QATCTAPHD. ...SPGTDLL EANLLW....
    HC C2 RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI EANLLWRQEM
    HC G9 RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI TANLLWRQEM
  HCU16326 RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI EANLLWRQEM
 HCV H CMR RGSPPSMASS SASQLSAPSL KATCTANHD. ...SPDAELI EANLLWRQEM
    HCV_J1 RGSPPSEASS SASQLSAPSL KATCTINHD. ...SPDAELI EANLLWRQEM
  HCV J483 RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI EANLLWRQEM
    HCV J8 RGSPPSQASS SASQLSAPSL KATCTTHKT. ...AYDCDMV DANLF....M
   HCV JK1 RGSPPSLASS SASQLSAPSL KATCTTRHD. ...SPDADLI EANLLWRQEM
    HCV JS RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI EANLLWRQEM
 HCV K1 R1 RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI EANLLWRQEM
 HCV K1 R2 RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI EANLLWRQEM
HCV_K1_R3 RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI EANLLWRQEM HCV_K1_S1 RGSPPSLASS SASQLSAPSS KATYITQYD. ...SPDFDLI EANLLWRQEM
HCV_K1_S2 RGSPPSLASS SASQLSAPSL KATCTTRHD. ...SPDADLI EANLLWRQEM
HCV_K1_S3 RGSPPSLASS SASQLSAPSL KATCTTCHD. ...SPDADLI EANLLWRQEM
    HCV_L2 RGSPPSLASS SASQLSAPSL KATCTTHHD. ...SPDADLI EANLLWRQEM
    HCV N RGSPPSLASS SASQLSAPSL RATCTTHSSY NLDSPDVDLI EANLLWRQEM
  HCV12083 KGSPPSLASS SANQLSAPSL RATCTTSQK. ...HPEMELL QANLLWKHEM
  HCV1480 RGSPPSLANS SASQLSAPSL KATCTIQGH. ... HPDADLI KANLLWRQCM
  HCVPOLYP RGSPPSLASS SASQLSAPSL KATCTTRHD. ...SPDADLI EANLLWRQEM
      HD 1 RGSPPSLASS SASQLSAPSL KATCTTRHD. ...SPDADLI EAHLLWRQEM
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     Th580 RGSPPSLASS SASQLSAPSL KATCTANGD. ... HPDAELI EANLLWRQEM
Type 3a CB RGSPPSEASS SASQLSAPSL KATCQTHRP. ... HPDAELV NANLLWRQEM
   TypeV D RGSPPSEASS SASQLSAPSL KATCQTHRP. ... HPDAELV DANLLWRQEM
     VN004
           RGSPPSLASS SASQLSAPSL KATCTMHGA. ... HPDAELI EANLLWRQEM
            RGSPPSLASS SASQLSAPSL KATCTTAGK. ... HPDAELI EANLLWRQEV
     VN235
           RGSPPSCASS LASQLSAPSL KATCTTHCA. ... HPDADLI EANLLWRQEV
     VN405
     BEBE1 GGNMTRIESE SKVLMVDSFD PVVDKE.DER EPSIPSEYLL PKS.RFPPAL
    D89815 GGNITRVESE NKIVILDSFE PLRAEE.DER EVSAAAEILR KTR.KFPAAM
ED43type_4 GSTATRVETD EKVIILDSFE SCVAEQNDDR EVSVAAEILR PTK.KFPPAL
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HC C2 GGNITRVESE NKVVILDSFE PLRAEE.DER EVSVAAEILR KTR.RFPPAM
    HC G9 GGNITRVESE NKIVILDSFD PLVAEE.DDR EISVPAEILL KSK.KFPPAM
 HCU16326 GGNITRVESE NKVVILDSFD PLRAED.DEG EISVPAEILR KSR.KFPPAL
 HCV H CMR GGNITRVESE NKVVILDSFD PLVAEE.DER EVSVPAEILR KSR.RFARAL
   HCV J1 GGNITRVESE NKVVILDSFD PLVAEE.DER EISVPAEILR KSR.RFTQAL
 HCV J483 GGNITRVESE NKVVILDSFE PLHAEG.DER EISVAAEILR KSR.KFPSAL
   HTV J8 GGDVTRIESD SKVIVLDSLD SMTEVE.DDR EPSVPSEYLI KRR.KFPPAL
  HCV JK1 GGNITRVESE NKVVILDSFE PLRAEE.DER EVSVAAEILR KSR.KFPPAL
   HCV JS GGNITRVESE NKVVILDSFD PLHAEE.DER EVSVAAEILR KSR.KFPPAL
HCV K1 R1 GGNITRVESE NKVIILDSFD PLRAEE.DER EVSIPAEILR KSK.KFPPAL
HCV K1 R2 GGNITRVESE NKVVILDSFE PLRAEE.DER EVSLPAEILR KSR.KFPRAM
HCV K1 R3
           GGNITRVESE NKVVILDSFD PLRAEE.DER EVSVAAEILR KTR.KFPPAL
HCV K1 S1
           GGNITRVESE NKVVTLDSFD PLRAEE.DER EVSIPAEILR KSK.KFPSAL
           GGNITRVESE NKVVILDSFE PLRAEE.DER EVSLPAEILR KSR.KFPPAM
HCV K1_S2
HCV K1 S3 GGNITRVESE NKVVILDSFD PLRAEE.DER EVSVAAEILR KTK.KFPPAL
   HCV L2
           GGNITRVESE SKVVILDSFD PLRAEE.GEG EVSVAAEILR KSK.KFPPAL
    HCV N GGNITRVESE NKVVVLDSFE PLRAEG.DEN EISIAAEILR KSK.KFPAAI
 HCV12083 GSHIPRVQSE NKVVVLDSFE LYPLEY.EER EISVSVECHR QPRCKFPPVF
  HCV1480 GGNITRVEAE NKVEILDCFK PLKEEE.DDR EISVSADCFK KGP.AFPPAL
  HCVPOLYP
           GGNITRVESE NKVVILDSFD PLRAEE.DER EVSVAAEILR KSR.RFPRAM
     HD_1 GGNITRVESE NKVVILDSFD PLRAEE.DER EVSVPAEILR KSR.KFPPAM
  HPCCGAA GGNITRVESE NKVVILDSFD PLVAEE.DER EVSVPAEILR KSR.RFAPAL
    HPCFG GSNITRVESE TKVVILDSFE PLRAEE.DDT ELSIPAECFK KPP.KYPPAL
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 HPCGENOM GGNITRVESE NKVVILDSFD PLRAEE.DER EVSVAAEILR KSR.KFPSAL
  HPCHUMR GGNITRVESE NKVVVLDSFD PLRAEE.DER EVSVPAEILR KSK.KFPAAM
     HPCJ GGNITRVESE NKVVILDSFE PIRAEE.DER EVSVPAEILR RSR.KFPAAM
   HPCJCG GGNITRVESE NKVVILDSFD PIRAVE.DER EISVPAEILR KPR.KFPPAL
 HPCJK046 GGNITRVESE NKIVILDSFE PLKAEF.DDR EISVAAECHR PPRFKYPPAL
  HPCJK049 GSNITRVESE SKVVILDSFE PLRACD.DED ELSVAAECFK KPP.KYPPAL
   HPCJTA GGNITRVESE NKVVILDSFD PLRAEE.DER EVSVAAEILR KSK.KFPPAL
   HPCJTB GGNITRVESE NKVVILDSFD PLRAEE.DER EVSVAAEILR KSK.KFPPAL
   HPCK3A GSNITRVESE TKVVILDSFE PLRAET.DDA ELSAAAECFK KPP.KYPPAL
           GGNITRVESE NKVVILDSFD PLVAEE.DER EISVPAEILR KSR.RFAQAL
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           GGDVTRIESE SKVVVLDSLD PMVEER.SDL EPSIPSEYML PKK.RFPPAL
  HPCPOLP
           GGNITRVESE NKIVILDSFE PLRAEE.DER EVSVAAEILR KTR.KFPAAM
    HPCPP
           GGNITRVESE NKVVILDSFD PLRAED.DEG EISVPAEILR KSR.KFPPAL
  HPCUNKCD
           GGNITRVESE NKIVILDSFE PLRAEE.DER EVSVAAEILR KTR.KFPAAM
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    NDM59
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           GSNITRVESE TKVVVLDSFE PLRAET.DDV EPSVAAECFK KPP.KYPPAL
     NZLI
           GGNITRVEAE NKVVILDSFE PLKADD.DDR EISVSADCFR RGP.AFPPAL
     SA13
           GSNITRVESE TKVVILDSFD PLVAEY.DDR EISVSAECHR PPRPKFPPAL
     Th580
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Type 3a CB
   TypeV D
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     VN405
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  HCU16326 PIWAPPDYNP PLLESWKDPD YVPPVVHGCP LPPTKAPPIP PPRRKR.TVV
 HCV_H_CMR PVWARPDYNP PLVETWKKPD YEPPVVHGCP LPPPRSPPVP PPRKKR.TVV
   HCV_J1 PIWARPDYNP PLIETWKKPN YEPPVVHGCP LPPPQSPPVP PPRKKR.TVV
  HCV_J483 PIWARPDYNP PLLESWKDPD YVPPVVHGCP LPPTKAPPIP PPRRKR.TVV
   HCV J8
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   HCV_JK1
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  HCV1480 PVWARPGYDP PLLETWKRPD YDPPQVWGCP IPPAGPPPVP LPRRKRKPME
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   HPCJTB PIWARPDYNP PLLESWKSPD YVPPAVHGCP LPPTTGPPIP PPRKKR.TVV
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   Type\overline{V} D
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    HC G9 LDESTVSSAL AELATKTFGS STT.SGVTSG EAAESSPAPS CD....GELD
  HCU16326 LTESTVSSAL AELATKTFGS SGS.SAIDSG TATAPPDQAS GD....GDRE
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   HCV J1 LTESTLSTAL AELAAKSFGS SST.SGITGD NTTTSSEPAP SG....CSPD
  HCV_J483 LTESNVSSAL AELATKTFSS SGS.SAVDSG TATALPDQAS DD....GDKG
   HCV J8 LTQDNVEGVL REMADKVLSP LQDNNDSGHS TGADTGGDIV QQPSD.ETAA
   HCV_JK1 LTESTVSSAL AELATKTFGS SGS.SAVDSG TATAPPDQPS DD....GDRG
   HCV JS LTESTVSSAL AELATKTFGS SGS.SAADSG TATAPPDQAS DD....GDKG
 HCV K1 R1 LTESTVSSAL AELATKTFGS SGS.SAADRG TATAPPDQAS ND....GDAG
 HCV_K1_R2 LTESTVSSAL AELATKTFGS SES.SAADSG TATAPPDQPS SD....GDAG
 HCV_K1_R3 LTESTVSSAL AELATKTFGS SGS.SAVDSG TATAPPDQTS ND....GDTG
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  HCV1480 LSDSTVSQVM ADLADARFKV DTP.SIEGQD SALGTSSQHD SGPEEKRDDN
 HCVPOLYP LTESTVSSAL AELATKTFGS SES.SAVDSG TATAPPDQPP DN....DDTG
     HD 1 LTESTVSSAL AELATKTFGS SES.SAVDSG TATAPPGQSS DD....VDTG
  HPCCGAA LTESTLPTAL AELATKSFGS SST.SGITGD NTTTSSEPAP SG....CPPD
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     SA13
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    Th580
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  TypeV D
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          LDSSNVSAAL AOLAAKTFET PSS.PTTGYG SDQPDHSTES SEHDRDDGVA
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    HC G9
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HCV H CMR
   HCV J1
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 HCV J483
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   HCV J8
  HCV_JK1
          SDDESYSSMP PLEGEPGDPD LS..............DGSWSTVS
   HCV JS
          SDVESYSSMP PLEGEPGDPD LS.............DGSWSTVS
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SDVESYSSMP PLEGEPGDPD LS................................DGSWSTVS
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        HPCJK049
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         TypeV D
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HCU16326	AKNEVFCVOP	EKGGRKPARL		CEKMALYDVV	· -
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TypeV_D		ARGGRKRARL			
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           VPLAKAAWET AKHSPVNSWL GNIIMYAPTL WARIVLMTHF FSVLQSQEQL
  HCV1480
           TPLARAAWET ARHTPVNSWL GNIIMYAPTL WARMILMTHF FSILLAQEQL
  HCVPOLYP
           TPLARAAWET ARHTSVNSWL GNIIMYAPTL WARMILMTHF FSILLAQEQL
     HD 1
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   HPCCGAA
           TPLARAAWET ARHTPVNSWL GNIIMFAPTI WVRMVLITHF FSILQAQEQL
    HPCFG
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HPCGENANTI
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  HPCGENOM
  HPCHUMR
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           TPLARAAWET ARHTPVNSWL GNIIMYAPTL WARMILMTHF FSILLAQEQL
     HPCJ
   HPCJCG
           TPLARAAWET VRHTPVNSWL GNIIMYAPTL WARMILMTHF FSILLAQEQL
  HPCJK046 NVLARAAWET ARHTPVNSWL GNIIMYAPTI WVRMVLMTHF FGILQPQEQL
  HPCJK049
           TPLARAAWET ARHTPVNSWL GNIIMYAPTI WVRMVIMTHF FSILQAQEQL
           TPLARAAWET ARHTPVNSWL GNIIMYAPTL WARMILMTHF FSILLAQEQL
   HPCJTA
           TPLARAAWET ARHTPVNSWL GNIIMYAPTL WARMILMTHF FSILLAQEQL
    HPCJTB
    HPCK3A TPLARAAWET ARHTPVNSWL GSIIMYAPTI WVRMVMMTHF FSILQSQEIL
 HPCPLYPRE TPLARAAWET ARHTPVNSWL GNIIMFAPTL WARMILMTHF FSVLIARDQL
           TPIARAAWET VRHSPVNSWL GNIIQYAPTI WARMVLMTHF FSILMAQDTL
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    HPCPP TPLARAAWET ARHTPVNSWL GNIIMYAPTL WARMILMTHF FSILLAQEQL
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     NDM59 TPLSRAAWET VRHSPVNSWL GNIIQYAPTI WVRMVLMTHF FSILMAQDTL
     NZLI TPLARAAWET ARHTPVNSWL GNIIMYAPTI WVRMVMMTHF FSILQSQEIL
      SA13 VPLARAAWET AKHSPVNSWL GNIIMYAPTL WARIVLMTHF FSVLQSQEQL
     Th580 TPLARAAWET ARHTPVNSWL GNIIMYAPTI WVRMVLMTHF FSILQCQEQL
Type_3a_CB
           TPLARAAWET ARHTPVNSWL GNIIMYAPTI WVRMVMMTHF FSILQSQEIL
           TPLARAAWET ARHTPVNSWL GNIIMYAPTI WVRMVMMTHF FSILQSQEIL
   TypeV D
            TPLARAAWET ARHTPVNSWL GNIIMYAPTI WVRMVLMTHF FQILQAQETL
     VN004
            TPLSRAAWET ARHTPVNSWL GNIIMYAPTI WVRMVLMTHF FAILQSQEIL
     VN235
            TPLSRAAWET ARHTPVNSWL GNIIMYAPAI WVRMVLMTHF FQILQAQEQL
     VN405
            2901
           DQDLNFEMYG AVYSVSPLDL PAIIERLHGL EAFSLHSYSP HELTRVAAAL
    BEBE1
    D89815
           EKALDCQIYG ATYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
           EKALDFDMYG VTYSITPLDL PAIIQRLHGL SAFTLHGYSP HELNRVAGAL
ED43type 4
    нс_<del>с</del>2
           EKALECQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
    HC G9 EKALDCEIYG AVHSVQPLDL PEIIQRLHGL SAFSLHSYSP GEINRVAACL
  HCU16326 EKTLDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
 HCV_H_CMR EQALNCEIYA ACYSIEPLDL PPIIQRLHGL SAFLLHSYSP GEVNRVAACL HCV_J1 EQALDCEIYG ACYSIEPLDL PPIIQRLHGL SAFSLHSYSP GEINRVAACL
  HCV_J483 EQALDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
    HCV_J8 NQNLNFEMYG AVYSVNPLDL PAIIERLHGL EAFSLHTYSP HELSRVAATL
   HCV JK1 EKALGCQIYG ATYFIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
    HCV JS EKALDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
 HCV K1 R1 EKALDCQIYG ACYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
 HCV K1 R2 EKALDCQIYG ACYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
HCV K1 R3 DKALDCQIYE AIYSIGPLDL PQVIQRLHGL SAFSLHSYSP GEINRVASCL
HCV_K1_S1 EKALDCQIYG ACYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
 HCV K1 S2 EKALDCQIYG ACYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
 HCV K1 S3 DKALDCQIYE AIYSIGPLDL PQVIQRLHGL SAFSLHSYSP GEINRVASCL
    HCV L2 EKALECQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
    HCV N EKALDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
  HCV12083 EKAFDFDIYG VTYSVSPLDL PAIIQRLHGM AAFSLHGYSP VELNRVGACL
  HCV1480 EKTLAFEMYG SVYSVTPLDL PAIIQRLHGL SAFSLHSYSP SEINRVASCL
  HCVPOLYP EKALDCQIYG ACYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
     HD 1 EKALDCQIYG ACYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
   HPCCGAA EQALNCEIYG ACYSIEPLDL PPIIQRLHGL SAFSLHSYSP GEINRVAACL
    HPCFG ERALDFEMYG ATYSVTPLDL PAIIERLHGL SAFSLHGYSP TELNRVAGAL
HPCGENANTI EKALDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
  HPCGENOM EKALDCQIYG AYYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
   HPCHUMR EKALDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
           GKALDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
      HPCJ
    HPCJCG EKALDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
  HPCJK046
           HKALDFDMYG VTYNITPLDL PQIIQRLHGM AAFSLHGYSP GELNRVGACL
           EKALDFEMYG AVYSVTPLDL PAIIERLHGL SAFSLHSYSP VELNRVAGAL
  HPCJK049
    HPCJTA EKALDCQIYG ACYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASCL
    HPCJTB EKALDCOIYG ACYSIEPLDL PQIIQRLHGL SAFSLHSYSP GEINRVASSL
    HPCK3A DRPLDFEMYG ATYSVTPLDL PAIIERLHGL SAFSVHSYSP VELNRVAGTL
           EOALDCEIYG ACYSIEPLDL PPIIQRLHGL SAFSLHSYSP GEINRVAACL
 HPCPLYPRE
   HPCPOLP DQNLNFEMYG AVYSVSPLDL PAIIERLHGL DAFSLHTYTP HELTRVASAL
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    HPCPP
           EKTLDCQIYG ACYSIEPLDL PQIIERLHGL SAFSLHSYSP GEINRVASCL
  HPCUNKCD
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    MKC1A
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      NZLI DRPLDFEMYG ATYSVTPLDL PAIIERLHGL SAFTLHSYSP VELNRVAGTL
      SA13 EKALAFEMYG SVYSVTPLDL PAIIQRLHGL SAFTLHSYSP SEINRVSSCL
     Th580 EAALNFDMYG VTYSVTPLDL PAIIQRLHGM AAFSLHGYSP TELNRVGASL
Type_3a_CB DRPLDFEMYG ATYSVTPLDL PAIIERLHGL SAFTLHSYSP VELNRVAGTL
   TypeV_D DRPLDFEMYG ATYSVTPLDL PAIIERLHGL SAFTLHSYSP VELNRVAGTL
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           HKALDFDMYG VTYSVTPLDL PYIIQRLHGM AAFSLHGYSP GELNRVASCL
     VN405
           DKVLDFDMYG VTYSVSPLQL PAIIQRLHGM AAFSLHGYSP TELNRVGACL
            2951
                                                                   3000
     BEBE1
            RKLGAPPLRA WKSRARAVRA SLISRGGSAA TCGRYLFNWA VRTKLKLTPL
    D89815
           RKLGVPPLRV WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VKTKLKLTPI
ED43type 4 RKLGVPPLRA WRHRARAVRA KLIAQGGRAK ICGIYLFNWA VKTKLKLTPL
     HC C2 RKLGVPPLRV WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VRTKLKLTPI
     HC G9 RKLGVPPLRA WRHRARSVRA TLLSQGGRAA ICGKYLFNWA VKTKLKLTPL
  HCU16326 RKLGVPPLRA WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VRTKLKLTPI
 HCV_H_CMR RKLGVPPLRA WRHRARSVRA RLLSRGGRAA ICGKYLFNWA VRTKLKLTPI
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 HCV_J1 RKLGVPPLRA WRHRARSVRA KLLSRGGRAA ICGKYLFNWA VRTKLKLTPI
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HCV_J8 RKLGAPPLRA WKSRARAVRA SLIAQGARAA ICGRYLFNWA VKTKLKLTPL
HCV_JK1 RKLGVPPLRV WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VRTKLKLTPI
HCV_JS RKLGVPPLRV WRHRARGVRA KLLSQGGRAA TCGKYLFNWA VRTKLKLTPI
HCV_K1_R1 RKLGVPPLRT WRHRARSVRA KLLSQGGRAA TCGRYLFNWA VKTKLKLTPI
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HCV_K1_R3 RKLGVPPLRV WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VKTKLKLTPI
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 HCV K1 S3 RKLGVPPLRV WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VKTKLKLTPI
    HCV L2 RKLGVPPLRV WRHRARRVRA KLLSQGGRAA TCGKYLFNWA VRTKLKLTPI
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   HPCCGAA RKLGVPPLRA WRHRAWSVRA RLLARGGKAA ICGKYLFNWA VRTKLKLTPI
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   HPCHUMR RKLGVPPLRV WRHRARSVRA RLLSQGGRAA TCGKYLFNWA VKTKLKLTPI
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    HPCJCG RKLGVPPLRV WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VKTKLKLTPI
  HPCJK046 RKLGAPPLRA WRHRARAVRA KLIAQGGKAA ICGMYLFNWA VKTKLKLTPL
  HPCJK049 RKLGIPPLRA WRHRARAVRA KLISQGGKAK ICGLYLFNWA VRTKAKLTPL
    HPCJTA RKLGVPPLRV WRHRARSVRA RLLSQGGRAA TCGKYLFNWA VRTKLKLTPI
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 HPCPLYPRE RKLGVPPLRA WRHRARSVRA RLLARGGRAA ICGKYLFNWA VRTKLKLTPI
           RKLGAPPLRA WKSRARAVRA SLISRGGRAA VCGRYLFNWA VKTKLKLTPL
   HPCPOLP
     HPCPP RKLGVPPLRV WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VKTKLKLTPI
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     MKC1A RKLGVPPLRV WRHRARSVRA KLLSQGGRAA TCGKYLFNWA VKTKLKLTPI
            RKLGAPPLRA WKSRARAVRA SLISRGGRAA ICGRYLFNWA VKTKLKLTPL
     NDM59
      NZLI RKLGCPPLRA WRHRARAVRA KLIAQGGKAK ICGLYLFNWA VRTKTNLTPL
      SA13 RKLGVPPLRA WRHRARAVRA KLIAQGGKAA ICGIYLFNWA VKTKRKLTPL
     Th580 RKLGAPPLRA WRHRARAVRA KLIAQGGKAA ICGKYLFNWA VKTKLKLTPL
Type_3a_CB RKLGCPPLRA WRHRARAGRA KLIAQGGKAK ICGLYLFNWA VRTKTKLTPL
            RKLGCPPLRA WRHRARAVRA KLIAQGGKAK ICGLYLFNWA VRTKTNLTPL
   TypeV D
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     VN004
            RKLGAPPLRA WRHRARAVRA KLIAQGGKHA ICGKYLFNWA VRTKLKLTPL
     VN235
            RKLGAPPLRA WRHRARAVRA KLIAQGGGAA ICGKYLFNWA VKTKLKLTPI
     VN405
             3001
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     BEBE1
           PEASQLDLSG WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
    D89815
            PAAAKLDLSG WFTVGAGGGD IYHSMSHARP RYLLLCLLIL TVGVGIFLLP
ED43type 4
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     HC_G9 PSASQLDLSN WFTGGYSGGD IYHSVSHVRP RWFFWCLLLL SVGVGIYLLP
  HCU16326 PAASRLDLSG WFVAGYSGGD IYHSLSRARP RWFMLCLLLL SVGVGIYLLP
 HCV H CMR AAAGRLDLSG WFTAGYSGGD IYHSVSHARP RWFWFCLLLL AAGVGIYLLP
    HCV J1 AAAGRLDLSG WFTAGYSGGD IYHSVSHARP RWFWFCLLLL AAGVGIYLLP
  HCV J483 PAASQLDLSG WFVAGYSGGD IYHSLSRARP RWFLLCLLLL SVGVGIYLLP
    HCV J8 PEASRLDLSG WFTVGAGGGD IYHSVSHARP RLLLLCLLLL SVGVGIFLLP
   HCV JK1 PAASQLDLSG WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
    HCV JS PAASRLDLSG WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
 HCV K1 R1 PAASQLDLSN WFVAGYSGGD VYHSLSRARP RWFMLCLLLL SVGVGIYLLP
 HCV K1 R2 PAASQLDLSG WFVAGYSGGD IYHSVSRARP RWFMWCLLLL SVGVGIYLLP
 HCV_K1_R3 PAASQLDLSS WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
HCV K1 S1 PAASQLDLSN WFVAGYSGGD VYHSLSRARP RWFMLCLLLL SVGVGIYLLP
HCV_K1_S2 PAASQLDLSG WFVAGYSGGD IYHSVSRARP RWFMWCLLLL SVGVGIYLLP
HCV_K1_S3 PAASQLDLSS WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
HCV_L2 PAASRLDLSS WFVAGYSGGD IYHSVSHARP RWFMLCLLLL SVGVGIYLLP
     HCV N PAASOLDLSG WFVAGYSGGD IYHSLSRARP RWFMLCLLLL SVGVGIYLLP
  HCV12083
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   HCV1480 ADADRLDLSS WFTVGAGGGD IYHSMSRARP RNLLLCLLLL SVGVGIFLLP
  HCVPOLYP PAASQLDLSN WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
      HD_1 PAAFQLDLSG WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
            TAAGRLDLSG WFTAGYSGGD IYHSVSHARP RWFWFCLLLL AAGVGIYLLP
   HPCCGAA
     HPCFG PTAGQLDLSS WFTVGVGGND IYHSVSRART RHLLLCLLLL TVGVGIFLLP
HPCGENANTI PAASQLDLSK WFVAGYGGGD IYHSLSRARP RWFMLCLLLL SVGVGIYLLP
  HPCGENOM PAASRLDLSG WFVAGYSGGD IYHSLSRARP RWFMLCLLLL SVGVGIYLLP
   HPCHUMR PAASRLDLSG WFVAGYSGGD IYHSLSRARP RWFMLCLLLL SVGVGIYLLP
      HPCJ PAASOLDLSS WFVAGYSGGD IYHSLSRARP RWFMLCLLLL SVGVGVYLLP
    HPCJCG PAASOLDLSG WFVAGYNGGD IYHSLSRARP RWFMLCLLLL SVGVGIYLLP
  HPCJK046 RDAHRLDLSG WFVAGYSGGD IFHSVSHARP RVLLLCLLLL TVGVGIFFLP
            PQAGLLDLSR WFTVGAGGND IYHSVSRARS RHLLLGLLLL TVGVGIFLLP
  HPCJK049
    HPCJTA PAASQLDLSS WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
            PAASOLDLSS WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
    HPCJTB
    HPCK3A PAAGQLDLSS WFTVGVGGND IYHSVSRART RYLLLCLLLL TVGVGIFLLP
 HPCPLYPRE AAAGQLDLSG WFTAGYSGGD IYHSVSHARP RWIWFCLLLL AAGVGIYLLP
            PEARLLDLSS WFTVGAGGGD IYHSVSRARP RLLLLGLLLL FVGVGLFLLP
   HPCPOLP
            PEASQLDLSG WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
     HPCPP
            PAASRLDLSG WFVAGYSGGD IYHSLSRARP RWFMLCLLLL SVGVGIYLLP
  HPCUNKCD
            PEASQLDLSG WFVAGYSGGD IYHSLSRARP RWFMWCLLLL SVGVGIYLLP
     MKC1A
            PEARLLDLSS WFTVGAGGGD IYHSVSRARP RLLLLSLLLL LVGVGLFLLP
     NDM59
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      NZLI
            ADADRLDLSS WFTVGAGGGD IYHSMSRARP RCILLCLLLL TVGVGIFLLP
      SA13
            AAASQLDLSG WFVAGYDGGD IYHSVSRARP RLLLLGLLLL TVGVGIFLLP
     Th580
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Type_3a_CB
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     VN004
     VN235
            RGAANLDLSG WFVSGGSGGD IFHSVSRARP RNLLLCLLLL TVGVGIFLLP
            PDAARLDLSG WFISGFSGGD IYHSVSRARP RIFLLCLLLL SVGVGIFLLP
     VN405
            3051
     BEBE1
            AR
    D89815
            NR
            AR
ED43type 4
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            NR
     HC G9
            NR
  HCU16326
            NR
 HCV H CMR
            NR
            NR
    HCV J1
            NR
  HCV J483
    HCV J8
            AR
   HCV_JK1
            NR
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HCV_JS
 HCV_K1_R1
 HCV_K1_R2
 HCV_K1_R3
 HCV_K1_S1
            NR
 HCV_K1_S2
 HCV_K1_S3
            NR
    HCV_L2
            NR
    HCV_N
            Ν.
  HCV12083
            AR
  HCV1480
            AR
  HCVPOLYP
            NR
      HD_1
            NR
   HPCCGAA
            NR
     HPCFG
            AR
HPCGENANTI
            NR
  HPCGENOM
            NR
  HPCHUMR
            NR
      HPCJ
            NR
    HPCJCG
            NR
            PR
  HPCJK046
  HPCJK049
            ΑŖ
    HPCJTA
            NR
    HPCJTB
    HPCK3A
 HPCPLYPRE
   HPCPOLP
     HPCPP
  HPCUNKCD
            NR
     MKC1A
            NR
     NDM59
            AR
      NZLI
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      SA13
            AR
     Th580
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Type_3a_CB
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   TypeV_D
            AR
     VN004
            AR
     VN235
            AR
     VN405
            AR
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Table 23. HIV Fusion Construct

(SEQ ID NO: 1934)

EP-HIV-1090 (SEQ ID NO: 1935)

MGMQVQIQSLFLLLLWVPGSRGKLVGKLNWAGAAILKEPVHGVNAACPKVSFEPIKIPIHYCAPA KAKFVAAWTLKAAAKAFPVRPQVPLGAAKLTPLCVTLGAAAVLAEAMSQVKVYLAWVPAHKG AAAAIFQSSMTKKTTLFCASDAKNIPYNPQSQGVVKHPVHAGPIANVTVYYGVPVWKKAAAQMA VFIHNFKNAAAYPLASLRSLFNLTFGWCFKLNRILQQLLFINAKIQNFRVYYRKAAVTIKIGGQLKK VPLQLPPLKAMTNNPPIPV

Table 24. HBV GCR-3697 Fusion Construct

GCR-3697	Polynucleotide
SEQ ID NO:[[]] 1936	1 Start ↑**** ATTGGCATGCAGGTGCAGATCCAGAGCCTGTTCCTGCTCCTGCTGTGGGTGCCAGGAAGCAGAGGCTTTCTC CTGTCCCTGGGCATCCACCTGAACGCCGCTGCAAAGTACACCAGCTTCCCCTGGCTGCTCAACGCCGCTGCC CGGTTCAGCTGGCCTGCCTGCTCGTGCCCTTCAACGCAGCCTTCCCCAGCTGCCTCAACGCCGCTGCC CGGTTCAGCTGGCTGTCCTGCTCGTCGCCCTTCAACGCAGCCTTCCCCCACTGCCTGGCCTTCAACGCCGCTGCC CGGTTCAGCTGGTCGACTTCTCCCAGTTCAGCCGGGGAGCCATCCTGCTCCTGTGCCTTAACGCTACATGA AAGCAGCCCTGGTGGTCGACTTCTCCCAGTTCAGCCGGGGAGCCATCCTGCTCCTGTGCCTAACTTTTTCTGCT CAACGCCCACACCCTGTGGGAAGGCTGCCATCTGTACCAACAAAACCTGGATAATATCTAGCG GACCCAGCCTGTACAAGGCATATCCAGCCCTGATGCCCCTGTACGCCTGCATCGGAGCTGCCCATTCAGCCATCAACGCCGCA GCCCTCTGGTGACCACCCTGAACGCCCTGATGCCCCTGTACGCCTCAACAGAACCCTGCCCATCAACACCCCCAAC CCATTCCTATCCCCTCCAACTGGGCCTTCAAAGGCAGCCGCCGCAACTCAACCCCCCAC TGCCCAGCGACTTCTTTCCCAGCTGGAAAGCCGCCGCGGTTCCTTCTGCAACAAAAAACACTTGGAGCTTTCGAACGCC CGCAGCCAACTTCTTCCCAGCTGGAAAGCCGCCGCGAGTACCCTTCGCCCTCGACTTCTTTCCCAGCTGGAAACC TGCCCAGCGACTTCTTTCCCAGCTGGAAACCCGCCCTAACAACACGCCGCCAACTTCACACCCCAACCTGAA GGCCGCAGCCAATCTCTGGCACACCGCTAGAAGCCGCCTTACAACACGCCGAACTTCTTTCCCAGCCTAGAAGC CGCAGCCAACTTCTTGGACACCGCTTGAACGCGCTTACAACAACACGTGGCCCAAAGTTCGCCCGAACCCAACCTGAA GGCCCCACAAAGTTCGTGGCCCGCCTTGGACCCTTGAAAGCCGCTTCCCTCGATTGTGAGCCGCCCAACTTCACA CGCCCCCCCAAAGTTCCTTGGCCCGCCTTGAACCCTTTCACAACCCCTTCCCCC GAACCACAATGGGACCAACGGAAGCACCCCCGCCCATGCCCCACCTTCCAACGCCCCTTCCACCTTCAACACCCCTTCCCCC GAACCACAATGGAACCACCTTCAACACCCTTCTTCTTTCT
GCR-3697	Polypeptide
SEQ ID NO:[[]] 1937	1 ↑ MGMQVQIQSLFLLLLWVPGSRGFLLSLGIHLNAAAKYTSFPWLLNAAARFSWLSLLVPFNAAFPHCLAFSYMKA ALVVDFSQFSRGAILLCLIFLLNAAAHTLWKAGILYKKAWMMWYWGPSLYKAYPALMPLYACIGAAAWLSLL VPFVNAAAGFLLTRILTINAAAIPIPSSWAFKAAAEYLVSFGVWNLPSDFFPSVKAAAFLPSDFFPSVKAAADLLD TASALYNSWPKFAVPNLKAAASAICSVVRRKLSLDVSAAFYNAAAKFVAAWTLKAAAKAANVSIPWTHKGAA GLSRYVARLNAAASTLPETTVVRRKHPAAMPHLLKAAARWMCLRRFIINASFCGSPYKAAYMDDVVLGVNAL WFHISCLTFKAAATPARVTGGVFKAAALTFGRETVLEYKQAFTFSPTYKNAGTSFVYVPSALNPADGPGPGLCQ VFADATPTGWGLGPGPGRHYLHTLWKAGILYKGPGPPGHHTALRQAILCWGELMTLAGPGPGESRLVVDFSQFS RGNGPGPGFFLLAQFTSAICSVVGPGPGLVPFVQWFVGLSPTVGPGPGLHLYSHPIILGFRKIGPGPGSSNLSWLSL DVSAAFGPGPGLQSLTNLLSSNLSWLGPGPGAGFFLLTRILTIPQSGPGPGVSFGVWIRTPPAYRPPNAPIGPGPGV GPLTVNEKRRLKLIGPGPGKQCFRKLPVNRPIDWGPGPGAANWILRGTSFVYVPGPGPGKQAFTFSPTYKAFLCG

Table 25. HBV AOSIb2 Fusion Construct

HBV AOSIb2	Polynucleotide
SEQ ID NO:[[]] 1938	1 Start ↑ ATG GGAATGCAGGTGCAGATCCAGAGCCTGTTTCTGCTCCTCTGTGGGTGCCCGGGTCCAGAGGACACAC CCTGTGGAAGGCCGGAATCCTGTATAAGGCCAAGTTCGTGGCTGCCTGGACCCTGAAGGCTGCCGCTTTCCT GCCTAGCGATTTCTTTCCTAGCGTGAACTTCCTGCTGTCCCTGGGAATCCACCTGTATATGGATGACGTGGTG CTGGGAGTGGGACTGTCCAGGTACGTGGCTAGGCTGTTCCTGCTGACCAGAATCCTGACCATCTCCACCCTG CCAGAGACCACCGTGGTGAGGAGGCAGGCCTTCACCTTTAGCCCTACCTA
HBV AOSIb2	Polypeptide
SEQ ID NO:[[]] 1939	T T MGMQVQIQSLFLLLLWVPGSRGHTLWKAGILYKAKFVAAWTLKAAAFLPSDFFPSVNFLLSLGIHLYMDDVVL GVGLSRYVARLFLLTRILTISTLPETTVVRRQAFTFSPTYKGAAAWLSLLVPFVNIPIPSSWAFKTPARVTGGVFKV GNFTGLYNLPSDFFPSVKTLWKAGILYKNVSIPWTHKGAALVVDFSQFSRNSAICSVVRRALMPLYACI \$\delta\$ 219

Table 26. HCV Fusion Construct

HCV 4312(1P) (SEQ ID NO: 1940)

MGMQVQIQSLFLLLLWVPGSRGRLGVRATRKKAAAKTSERSQPRNLPGCSFSIFNDLMGYIPLVK YLLPRRGPRLNTLCGFADLMGYRMYVGGVEHRKLLFNILGGWVKAAALADGGCSGGAYRLIVFP DLGVKFWAKHMWNFIGVAGALVAFKKQLFTFSPRRNGYLVAYQATVAAALLFLLLADALIFCHS KKKYLVTRHADVLGFGAYMSKCTCGSSDLYHMWNFISGIFWAKHMWNFKKAAAVLVGGVLAA AFLLLADARVLSAFSLHSYILAGYGAGVWMNRLAFANAAAKFVAAWTLKAAA

(SEQ ID NO: 1941)

GAATTCGCCGCCACCATGGGAATGCAGGTGCAGATCCAAAGCCTGTTTCTGCTCCTCTGTGG GTGCCCGGCTCCAGAGGAAGGCTGGGCGTGAGAGCCACCCGGAAGAAGGCTGCCGCTAAAAC AAGCGAGCGCTCCCAGCCCAGGAACCTGCCTGGATGCTCTTTCAGCATCTTTAATGACCTCAT GGGGTACATTCCACTGGTGAAGTATCTGCTCCCCAGACGGGGCCCTCGCCTGAACACTCTCTG TGGATTTGCTGATCTGATGGGGTACAGGATGTATGTCGGCGGAGTCGAACACAGAAAACTGCT CTTCAACATCCTGGGCGGATGGGTGAAGGCTGCCGCTCTGGCCGACGGGGGATGCAGCGGCG GAGCTTACAGGCTCATTGTCTTTCCCGATCTCGGAGTCAAATTTTGGGCAAAGCACATGTGGA ATTTCATCGGGGTGGCCGGAGCCCTGGTCGCTTTTAAAAAGCAGCTCTTCACCTTCTCCCCAA GACGGAACGGATACCTCGTCGCCTACCAGGCCACTGTGGCTGCAGCTCTGCTCTTCCTGCTCC TGGCCGATGCACTCATCTTCTGCCATTCCAAGAAAAAGTATCTGGTCACCAGACATGCTGACG TGCTGGGGTTTGGCGCCTACATGAGCAAGTGCACCTGTGGCAGCTCCGACCTGTATCACATGT GGAACTTTATTTCTGGAATCTTTTGGGCCAAGCACATGTGGAATTTTAAGAAAGCCGCTGCAG TCCTGGTGGCGCGCTCCTGGCAGCCGCTTTCCTGCTCCTGGCAGACGCCAGGGTGCTGTCTG CCTTCAGCCTCCACTCCTACATCCTCGCAGGGTATGGCGCAGGCGTGTGGATGAATCGGCTGA TCGCCTTTGCCAATGCTGCAGCTAAATTCGTGGCAGCCTGGACACTGAAAGCAGCTGCATGAG **GATCC**

Table 27. Plasmodium falciparum Fusion Construct

Pf33 (SEQ ID NO: 1942)

MGMQVQIQSLFLLLLWVPGSRGRLGVRATRKKAAAKTSERSQPRNLPGCSFSIFNDLMGYIPLVK YLLPRRGPRLNTLCGFADLMGYRMYVGGVEHRKLLFNILGGWVKAAALADGGCSGGAYRLIVFP DLGVKFWAKHMWNFIGVAGALVAFKKQLFTFSPRRNGYLVAYQATVAAALLFLLLADALIFCHS KKKYLVTRHADVLGFGAYMSKCTCGSSDLYHMWNFISGIFWAKHMWNFKKAAAVLVGGVLAA AFLLLADARVLSAFSLHSYILAGYGAGVWMNRLAFANAAAKFVAAWTLKAAA

(SEQ ID NO: 1943)

GCCGCCACCATGGGAATGCAGGTGCAGATCCAGAGCCTGTTTCTGCTCCTCTGTGGGTGCCC GGATCCAGAGGATTTATGAAAGCTGTCTGTGTAGAGGTGAATGTAACATGCGGTAACGGAAT TCAGGTGAGAAAGGGACTCATCATGGTACTCAGCTTTCTGAACGCAGCCCTGTTCCACATCTT TGACGGAGACAATGAAATCAAAGCCGCATTGCTCGCCTGTGCCGGACTAGCCTATAAAAAGA GTTTCCTTTTCGTTGAAGCACTATTTAACGCAGCACCCAGTGACGGTAAATGCAACCTATATA AAGCAGCTCAGACTAATTTCAAAAGCCTGTTAAGAAATCTGCCCTCAGAGAATGAAAGGGGT TACAAAGCCGCCGGCGTGTCCGAGAATATTTTCCTGAAGAACGCCGCTGCTTATTTTATACTC CATATGCGGCGAGCCGGCTCCTTTCAAGGCTGCAGCAAAATACAAGCTTGCCACATCAGTAT TGAAAGCAGCTGTTTTTTGATATTCTTTGATCTTTTTTTAAACTACTACATACCTCATCAGTCT AGTCTTAAAGCAGCCGGGCTACTGGGGGAACGTCTCTACTGTGGGGGCCGTCTTACTTGGAGGA GTTGGCCTCGTGTTGAACCTCGCGTGCGCAGGTCTGGCCTACAAAAAAGCGAAATTCATCAAG TCTCTGTTCCACATTTTTAAAGCCGCATTCTATTTCATACTAGTGAACCTTCTCAAAGCTTTCCT GATCTTCTTCGATCTATTCCTCGTAAAAGCGCTATTCTTCATTATCTTTAACAAAAATTATTAC GGCAAGCAAGAAATTGGTACTCACTCAAGTTTGTAGAAGCTCTGTTCCAGGAATACAACGCC GCTGCTAAATTCGTTGCAGCTTGGACCCTGAAAGCAGCTGCAAAGATCCTATCGGTCTTCTTTC TCGCTAATGCCGTATTAGCAGGACTTCTAGGCAACGTGAACTTTCAAGACGAAGAGAATATAG GCATCTACAAAGCCGCAGCACTGTACATTTCATTCTACTTCATCAAGGCCTTCATACTGGTCAA CCTTCTGATATTTCATAATGCAGCACTGCCATATGGGAGAACCAACTTGAAAGCGGCCCACGT GTTGAGCCACAACTCCTACGAGAAGAACGCCGCCGCGAAATATCTCGTCATTGTCTTCCTGAT **TTGA**

Table 28. Mycobacterium tuberculosis Fusion Construct

TB.1 (SEQ ID NO: 1944)

MQVQIQSLFLLLLWVPGSRGRMSRVTTFTVKALVLLMLPVVNLMIGTAAAVVKALVLLMLPVGA GLMTAVYLVGAAAMALLRLPVKRMFAANLGVNSLYFGGICVGRLPLVLPAVNAAAAKFVAAWT LKAAAKAAARLMIGTAAAGFVVALIPLVNAMTYAAPLFVGAAAAMALLRLPLV

(SEQ ID NO: 1945)

ATGCAGGTGCAGATCCAGAGCCTGTTTCTGCTCCTCTGTGGGTGCCCGGATCCAGAGGAAGG
ATGAGCAGAGTGACCACATTCACTGTCAAGGCCCTGGTGCTCCTGATGCTCCCCGTCGTGAAC
CTGATGATCGGCACCGCTGCAGCCGTCGTGAAAGCTCTCGTCCTCATGCTCCCTGTGGGA
GCAGGGCTGATGACAGCCGTGTACCTGGTCGCGCGTGCAGCCATGGCCCTCCTGCGGCTGCCA
GTGAAGCGCATGTTTGCTGCAAATCTGGGAGTCAACTCCCTCTATTTCGGGGGCATTTGCGTG
GGAAGGCTGCCCCTCGTGCTGCCTGCTGAATGCAGCCGCTGCCAAATTTGTCGCCGCTTGG
ACTCTGAAGGCAGCCGCTAAGGCCGCTGCAAGACTGATGATCGGGACCGCCGCTGCCGGCTT
CGTGGTCGCCCTGATTCCCCTGGTGAACGCCATGACATACGCAGCTCCTCTGTTTGTGGGAGC
CGCTGCAGCCATGGCTCTCCTGCGGCTGCCACTGTGTGA

Table 29. Hepatitis B Virus Core Protein (SEQ ID NO: [_]] 1946)

MQLFHLCLIISCSCPTVQASKLCLGWLWGMDIDPYKEFGATVELLSFLPSDFFPSVRDLLDTAS ALYREALESPEHCSPHHTALRQAILCWGELMTLATWVGVNLEDPASRDLVVSYVNTNMGLKF RQLLWFHISCLTFGRETVIEYLVSFGVWIRTPPAYRPPNAPILSTLPETTVVRRRGRSPRRRTP SPRRRRSQSPRRRRSQSRESQC

WHAT IS CLAIMED IS:

- 1. A method for identifying a candidate peptide epitope which induces a HLA class I CTL response against variants of said peptide epitope, comprising
 - a) identifying, from a particular antigen of an infectious agent, variants of a
 peptide epitope 8-11 amino acids in length, each variant comprising primary
 anchor residues of the same HLA class I binding motif; and
 - b) determining whether one of said variants comprises only conserved nonanchor residues in comparison to at least one remaining variant, thereby identifying a candidate peptide epitope.
- 2. A method for identifying a candidate peptide epitope which induces a HLA class I CTL response against variants of said peptide epitope, comprising
 - a) identifying, from a particular antigen of an infectious agent, variants of a
 peptide epitope 8-11 amino acids in length, each variant comprising primary
 anchor residues of the same HLA class I binding motif;
 - determining whether each of said variants comprises conserved, semiconserved or non-conserved non-anchor residues in comparison to each of the remaining variants; and
 - c) identifying a variant which comprises only conserved non-anchor residues in comparison to at least one remaining variant.
- 3. A method for identifying a candidate peptide epitope which induces a HLA class I CTL response against variants of said peptide epitope, comprising
 - a) identifying, from a particular antigen of an infectious agent, a population of variants of a peptide epitope 8-11 amino acids in length, each peptide epitope comprising primary anchor residues of the same HLA class I binding motif;
 - b) choosing a variant selected from the group consisting of:
 - a variant which comprises preferred primary anchor residues of said motif; and
 - ii) a variant which occurs with high frequency within the population of variants; and

- c) determining whether the variant of (b) comprises only conserved nonanchor residues in comparison to at least one remaining variant, thereby identifying a candidate peptide epitope.
- 4. A method for identifying a candidate peptide epitope which induces a HLA class I CTL response against variants of said peptide epitope, comprising
 - a) identifying, from a particular antigen of an infectious agent, a population of variants of a peptide epitope 8-11 amino acids in length, each peptide epitope comprising primary anchor residues of the same HLA class I binding motif;
 - b) choosing a variant selected from the group consisting of:
 - a variant which comprises preferred primary anchor residues of said motif; and
 - ii) a variant which occurs with high frequency within the population of variants; and
 - c) determining whether the variant of (b) comprises conserved, semi-conserved or non-conserved non-anchor residues in comparison to each of the remaining variants; and
 - d) identifying a variant which comprises only conserved non-anchor residues in comparison to at least one remaining variant.
- 5. The method of claim 1, wherein (b) comprises identifying a variant which comprises only conserved non-anchor residues in comparison to at least 25%, at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% of the remaining variants.
- 6. The method of claim 2 or 3, wherein (c) comprises identifying a variant which comprises only conservative non-anchor residues in comparison to at least 25%, at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% of the remaining variants.
- 7. The method of claim 4, wherein (d) comprises identifying a variant which comprises only conservative non-anchor residues in comparison to at least 25%, at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% of the remaining variants.

- 8. The method of any of claims 1-4, wherein (a) comprises aligning the sequences of said antigens.
- 9. The method of claim 3 or 4, wherein (b) comprises comprises choosing a variant which comprises preferred primary anchor residues of said motif.
- 10. The method of claim 3 or 4, wherein (b) comprises comprises choosing a variant which occurs with high frequency within said population.
- 11. The method of claim 10, wherein (b) comprises ranking said variants by frequency of occurrence within said population.
- 12. The method of claim 3 or 4 wherein (b) comprises choosing a variant which comprises preferred primary anchor residues of said motif and which occurs with high frequency within said population.
- 13. The method of claim 12, wherein (b) comprises ranking said variants by frequency of occurrence within said population.
- 14. The method of any of claims 1-13, wherein the identified variant comprises the fewest conserved anchor residues in comparison to each of the remaining variants.
- 15. The method of any of claims 1-4, wherein the remaining variants comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 27, 28, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 220, 240, 260, 280, or 300 variants.
- 16. The method of any of claims 1-15, wherein the infectious agent is selected from the group consisting of: HIV, HBV, HCV, HPV, Plasmodium falciparum, Influenza virus, and Dengue virus, Epstein-Barr virus, Mycobacterium tuberculosis, Chlamydia, Candida albicans, Cryptococcus neoformans, Coccidoides spp., Histoplasma spp, Aspergillus fumigatis, Plasmodium spp., Trypanosoma spp., Schistosoma spp., and Leishmania spp.
- 17. The method of claim 16, wherein the infectious agent is selected from the group consisting of: HIV, HBV, HCV, HPV, *Plasmodium falciparum*, Influenza virus, and Dengue virus.
- 18. The method of claim 16, wherein the infectious agent is HIV and the antigen is selected from the group consisting of: Gag, Env, Pol, Nef, Rev, Tat, Vif, Vpr, and Vpu.

- 19. The method of claim 16, wherein the infectious agent is HBV and the antigen is selected from the group consisting of: Pol, Env, Core, and NS1/Env2.
- 20. The method of claim 16, wherein the infectious agent is HCV and the antigen is selected from the group consisting of: Core, E1, E2, NS1, NS2, NS3, NS4, and NS5.
- 21. The method of claim 16, wherein the infectious agent is HPV and the antigen is selected from the group consisting of: E1, E2, E3, E4, E5, E6, E7, L1, and L2.
- 22. The method of claim 16, wherein the infectious agent is *Plasmodium falciparum* and the antigen is selected from the group consisting of: CSP, SSP2, EXP1, LSA1.
- 23. The method of any claims 1-4, wherein the selected variant and the at least one remaining variant comprise different primary anchor residues of the same motif or supermotif.
- 24. The method of any of claims 1-4, wherein the motif or supermotif is selected from the group consisting of those in Tables 1-2.
- 25. The method of any of claims 1-4, wherein the conserved non-anchor residues are at any of positions 3-7 of said variant.
- 26. The method of any of claims 1-4, wherein the variant comprises only 1-3 conserved non-anchor residues compared to at least one remaining variant.
- 27. The method of any of claims 26, wherein the variant comprises only 1-2 conserved non-anchor residues compared to at least one remaining variant.
- 28. The method of any of claims 27, wherein the variant comprises only 1 conserved non-anchor residue compared to at least one remaining variant.
- 29. The method of claim 16, wherein the infectious agent is HPV, and further wherein, the HPV infectious agent is selected from the group consisting of HPV strains 16, 18, 31, 33, 45, 52, 56, and 58.
- 30. The method of any of claims 1-29, wherein the variants are a population of naturally occurring variants.

METHODS OF IDENTIFYING OPTIMAL VARIANTS OF PEPTIDE EPITOPES ABSTRACT OF THE DISCLOSURE

The present invention is directed to methods for selecting a variant of a peptide epitope which induces a CTL response against another variant(s) of the peptide epitope, by determining whether the variant comprises only conserved residues, as defined herein, at non-anchor positions in comparison to the other variant(s). The present invention is also directed to variants identified by the methods above; peptides comprising such variants; nucleic acids encoding such variants and peptides; cells comprising such variants, and/or peptides, and/or nucleic acids; compositions comprising such variants, and/or peptides, and/or nucleic acids, and/or cells; as well as therapeutic and diagnostic methods for using such variants, peptides, nucleic acids, cells, and compositions.

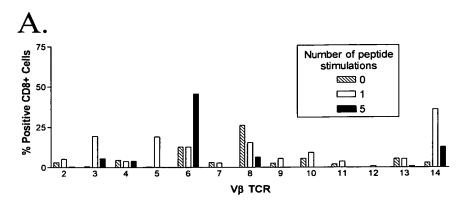
FIGS. 1A-1C

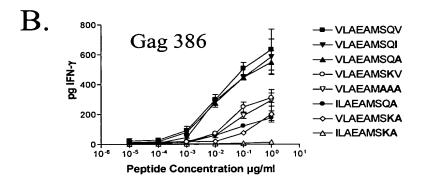
	Binding	# Isolates	Immunogenicity (SU)
	Amino Acid Sequence IC50 (nM)	Total B C 134 19 55	10 100 1000 10000
٨	P K L T P L C V T L 77.0 A K I T P L C V T L 461.2	2	
A.	KMTPLCVTL 44.7	1 1	E
	KLTPLCVTM 340.3	1	
	NA R L T P L C V T L 27.6	3 3	
	QLTPLCVTL 63.6 ELTPLCVTL 7190	5 1 3 1	D
	KLTFLCVTL 19.4	1	
	KLTSLCVTL 91.0	1 1	H
	KLTQLCVTL 23.8	1 1	
	K L T P F C V T L 87.3 K L T P R C V T L 597.0	1 1	ľ
	K L T P R C V T L 597.0 K L T P L C I T L 1.7	1	
	KLTPLCVPL 14.6	1 1	
	KLTPLCV S L 67.2	1	
	KLTPLCVAL 208.6	3	
	K L T P L C V I L 356.2 M Q I T P L C V T L 975.9	1	
	QMTFLCVQM 3153	3	
	KMTFLCVQM 1793	1	1
			10 100 1000 10000
	P VLAEAMSQV 49.9	54 15 3	
В.	A V L A E A M S Q A 23.8	67 1 36	
ъ.	VLAEAMSQT 289.6	11 9	
	VLAEAMSQI 70.9	1 1	
	NA I L A E A M S Q V 38.0 V L A E A M G Q V 55.3	5 3 1 1	
	VLAEAMSRV 39.8	1 1	**************************************
	V L A E A M S K V 230.5	1 1	30°C-00000000000000000000000000000000000
	VLAEAMSHV 29.3	2	
	M A L A E A M S Q A 15.0 I L A E A M S Q A 29.3	1 1 3 2	
	V L G E A M S Q A 176.0	1 1	<u> </u>
	VLAEAMSKA 69.4	1 1	
	VLAEAMSRA 127.4	1	· ·
	VLAEAMSHA 148.8	6 4 1 1	
	V L A E A M S H T 243.5 V L A E A M S A A 23.9	1	******************* =
	VLAEAMATA 6.7	1	
	V L A E A M A A A 17.2	1	H
	I LAEAMSKA 72.4	1 1	
	I LAEAMASA 22.2	1	
			10 100 1000 10000
\sim	PRILQQLLFI 72.5	86 15 28	
C.	ARLLQQLLFI 27.0	2 1	
	R T L Q Q L L F I 151.6 R M L Q Q L L F I 14.7	10 2 4 4 1 3	
	RVLQQLLFI 27.1	3 3	
	RILQQLLFV 27.7	21 2	
	RILQQLLFT 1427	6 2 1	
	R I L Q Q L L F A 122.9 NA K I L Q Q L L F I 40.5	2 1	
	TILQQLLFI 94.6	1	
	RILQQMILFI 186.7	1	
	R I L Q Q P L F I 140.1 R I L Q Q L L L I 199.2	1 1	
	R L Q Q L L L 199.2 M R V L Q Q L L F V 10.2	1 1	3
	RMLQQLLFV 21.5	2	
	RMLQQLLFT 125.7	1 1	
	RTLQQLLFA 948.4	1 1	
	RTLQQLLFT 9708 RTLQQLLFV 120.4	1 10 1	
	RTLQQLMFI 143.1	1 1	<u> </u>
	RMLQHLLFI 15.7	1 1	₽
	RILQHLLFA 160.3	1	
	RILQRLLFV 64.0 RTLQLLLFV 4.7	1 1	
	115 1 L V2 L L L 1 7 T17		· • · · · · · · · · · · · · · · · · · ·

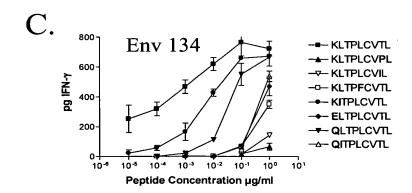
FIGS. 1D-1E

	 	Binding	# Is	olates			lmmunoge	nicity (SU)	
	Amino Acid Sequence	IC50 (nM)	Total		:	10	100	1000	10000
\mathbf{r}	PVTIKIGGQLK	15.5	18	13 1	_				
D.	AVAIKIGGQLK	151.3	2	1			1		
	VTIKIGGQLR	64.0	2					4	
	NAVTVKIGGQLK	60.7	11	1					
	VTIRIGGQLK	14.4	3	2				1	
	VTIKVGGQLK	59.4	2	2					
	VTIKIEGQLK	69.4	2	1					
	VTIKIGGQIK	183.5	1	•					
	2NA V T V K I G G Q L R	194.1	3					<u> </u>	
	VTVKIGGELK	39.2	1						
	VTVKIEGQLK	23.2	4				3-1		
	VTVKVGGQLK	54.3	3						
	VTVRIGGQLK	15.2	6						
	VTIRIGGQLR	22.9	2			description of			
	VTIRVGGQLK	13.2	1			-	-		
	VAIKIGGQIK	940.2	i	1		[]			
	VNIKVGGQLK	1768	i	, 1		1			
	VTIKIGGQIR	388.5	1	,					
	3NA V T I K L G G Q I R	219.5	- i -						
	VTVKIEGQLR	143.0	4			—			
	VTVKVGGQLR	198.7	2						
	VTIRVGGQLR	17.3	1			H			
	VSIKVGGQIK	85.9	30	30	0	-	33 4		
	VTVRVGGQLK	19.3	1	-	-	H			
	4NA V T I R V A G Q V K	20.8	1			1			
	VSIRVGGQTK	20.9	1			}			
	VSIRVGGQIK	90.6	4	4	Į.				
	VSIKVGGQIR	1339	6	6					
	VTVRIGGMQK	13.4	1						
	VSIRVGGQTR	240.6	1	1					
	ITVKIGKEVR	12904	1			1			
	1								
						10	100	1000	10000
\mathbf{C}	PVTVYYGVPVW	K 9.2	99	21 30	0				
E.	AVTVYYGVPVW		40	18	В			=-	
	NAVTIYYGVPVW	K 2.5	1						
	VTVYDGVPVW	K 18.8	1	1					
	VTVYYGVPIW	K 2.3	2						
	MITVYYGVPVW		1						
	V T I Y Y G V P V W I	R 3.0	1					⊣	
	V T V Y D G V P V W I	R 245.7	1	1		**********			
	V T V Y Y G I P V W I	R 16.7	1			***************************************		-1	
	VTVYYGVPVRI	R 270.7	1						
							-		_

FIGS. 2A-2C







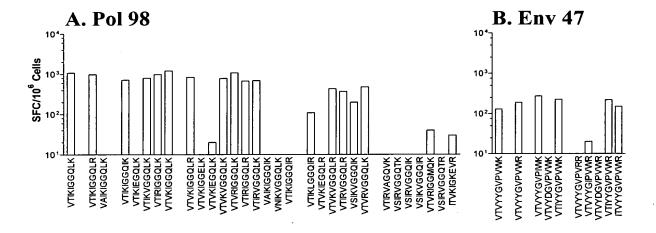


FIG. 4

	Binding		Predicted Cr	oss-reactivity	Immui	nogenicity (SU)
Amino Acid Sequence	IC ₅₀ (nM)	# Isolates	MTNNPPIPV	MTSNPPIPV	10 100	1000 10000
MTSNPPIPV	52.8	60	-	+	1	
MTNNPPIPV	128.4	33	+	+		≟ ⊣
M T S N P P V P V	21.8	26	-	+		3 ⊣
MTGNPPIPV	125.1	15	-	+		⊐≘⊣
M T G N P P V P V	2021	9	-	+	<u></u>	
M T N N P P V P V	85.6	6	+	+		 -
MTANPPVPV	20.0	3	-	+		H
MTHNPPIPV	167.0	2	+	-		
MTANPPIPV	2.3	1	<u> -</u>	+		
MTSDPPIPV	107.4	1	-	+	— —	
MTGNPSIPV	15.8	1	-	+	. ⊢	
MTGNPAIPV	1200	1	-	+		■ MTNNPPIPV
MTSNPAIPV	1465	1	-	+	 	DMTSNPPIPV
M T R N P P V P V	9171	1	-	-	J	